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(54) **MICROFABRICATED SURFACE NEUROSTIMULATION DEVICE AND METHODS OF MAKING AND USING THE SAME**

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None
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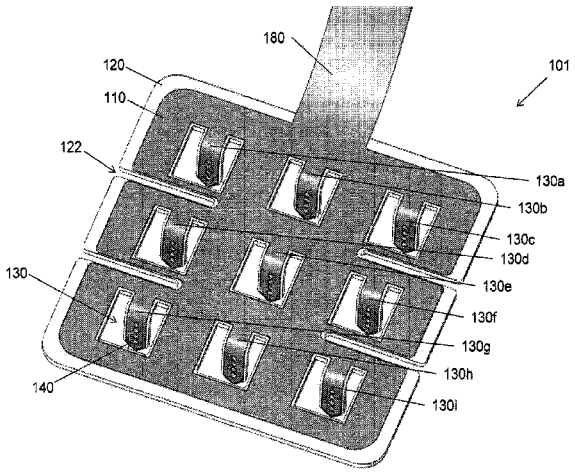
(57) **ABSTRACT**

Described herein are microelectrode array devices, and methods of fabrication and use of the same, to provide highly localized and efficient electrical stimulation of a neurological target. The device includes multiple microelectrode elements arranged along an supportive backing layer. The microelectrode elements are dimensioned and shaped so as to target individual neurons, groups of neurons, and neural tissue as may be located in an animal nervous system, such as along a region of a cortex of a human brain. Beneficially, the neurological probe can be used to facilitate location of the neurological target and remain implanted for long-term monitoring and/or stimulation.

19 Claims, 49 Drawing Sheets



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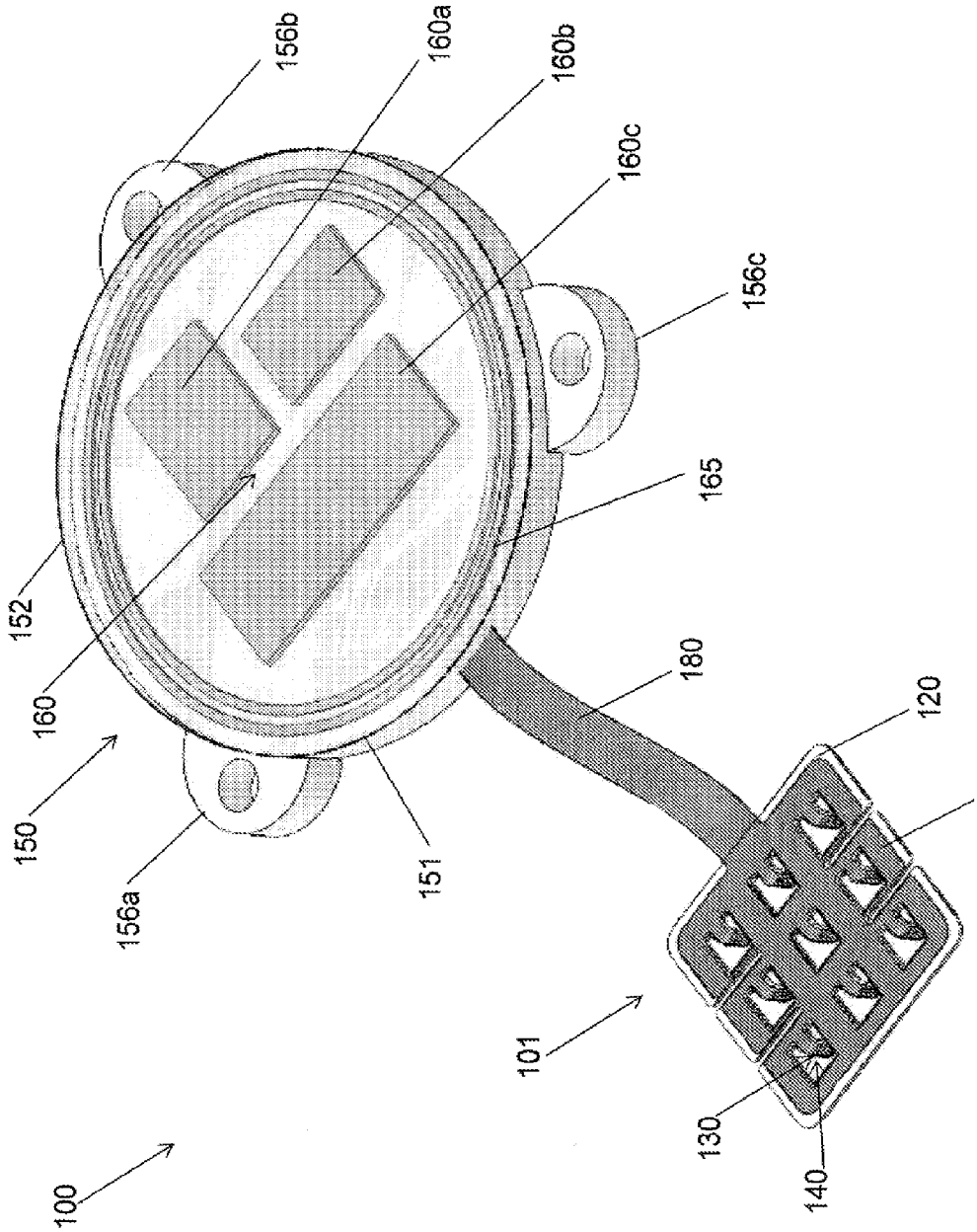
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160b
160c
156c
165
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160
180
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110
150
151
156a
101
130
140
100

FIG. 1

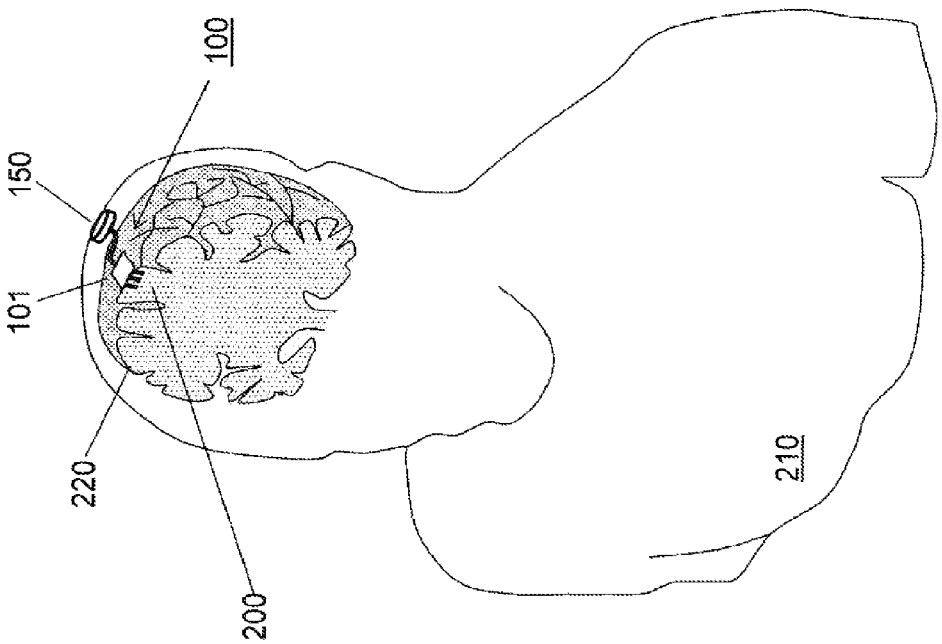


FIG. 2

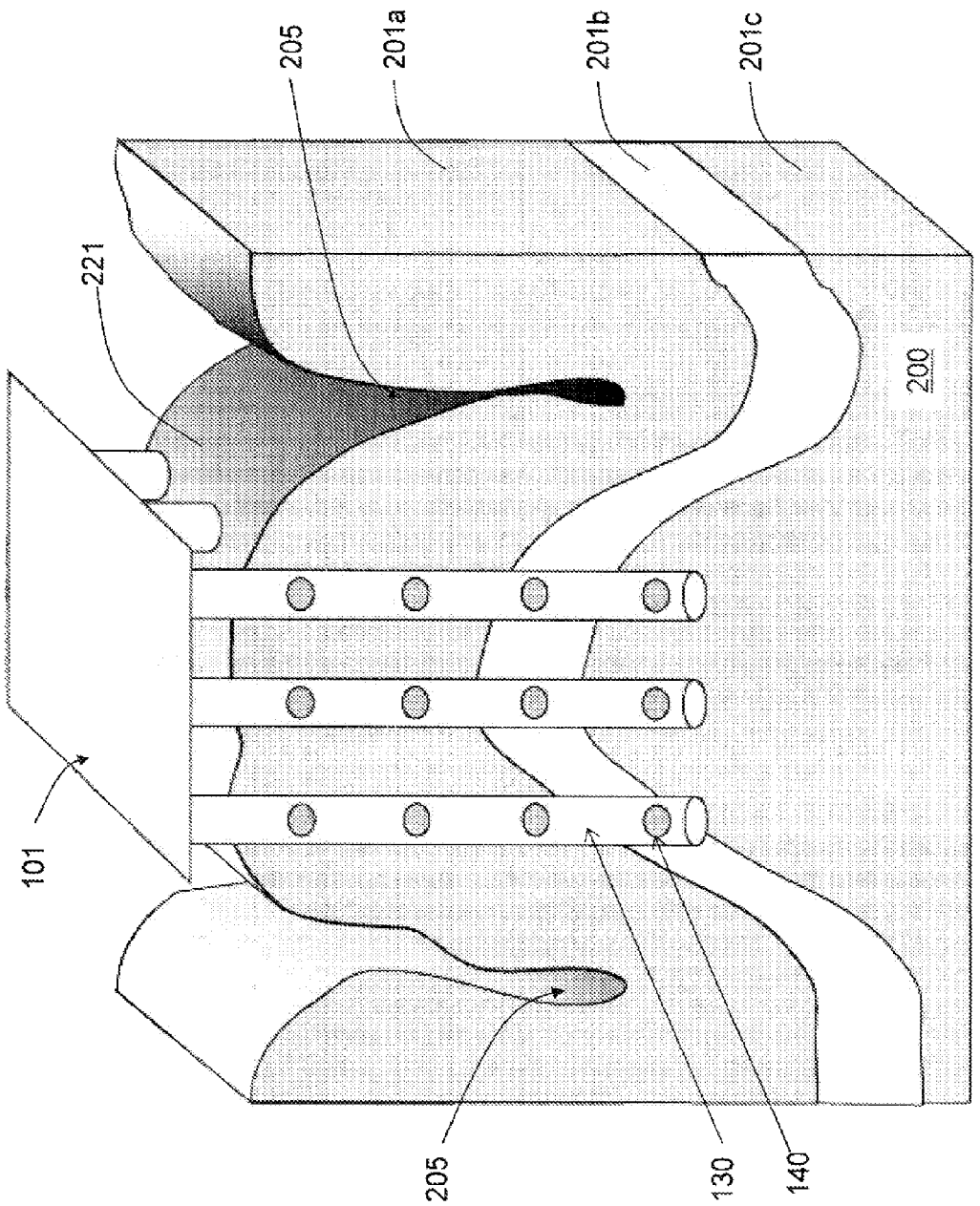
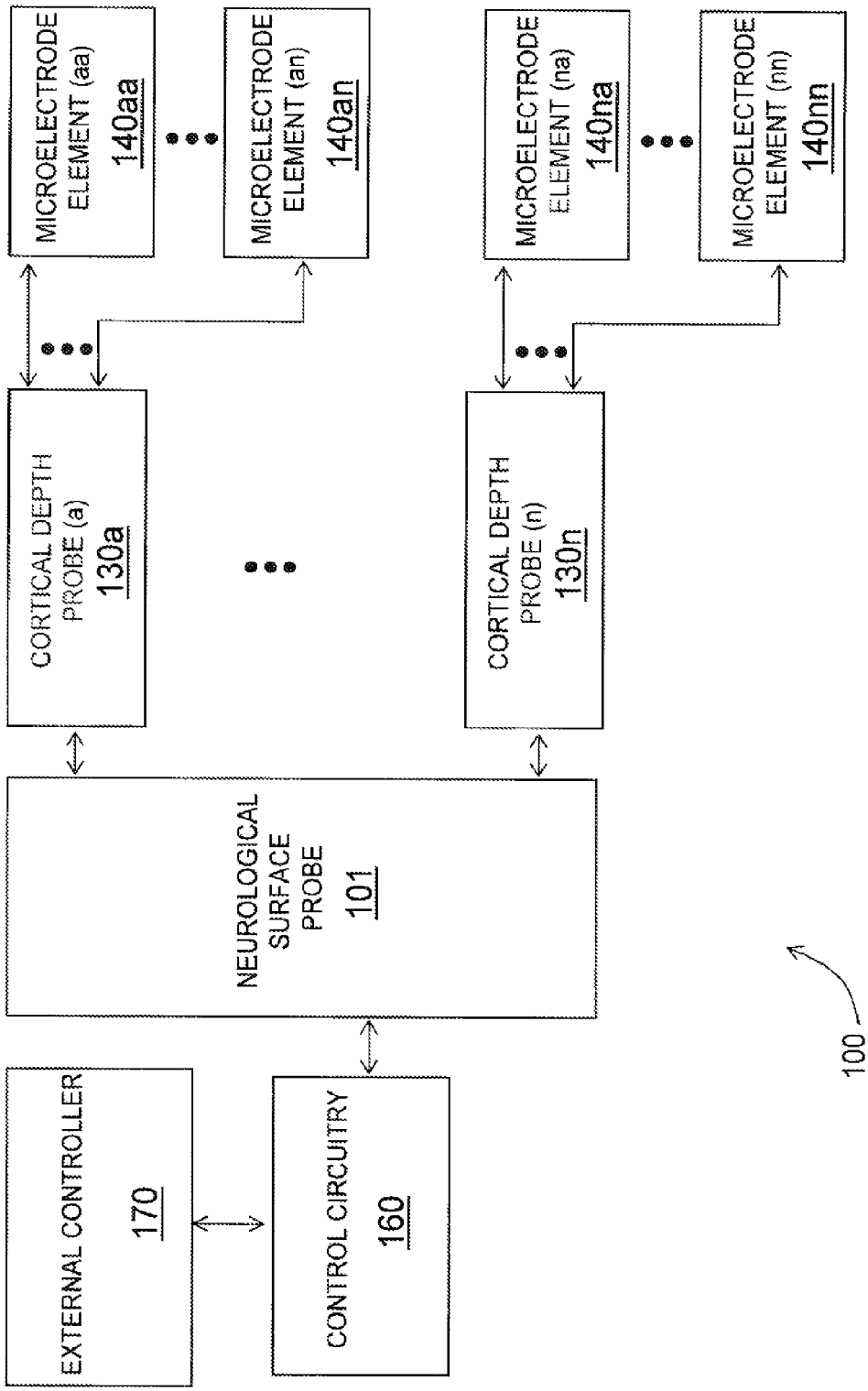


FIG. 3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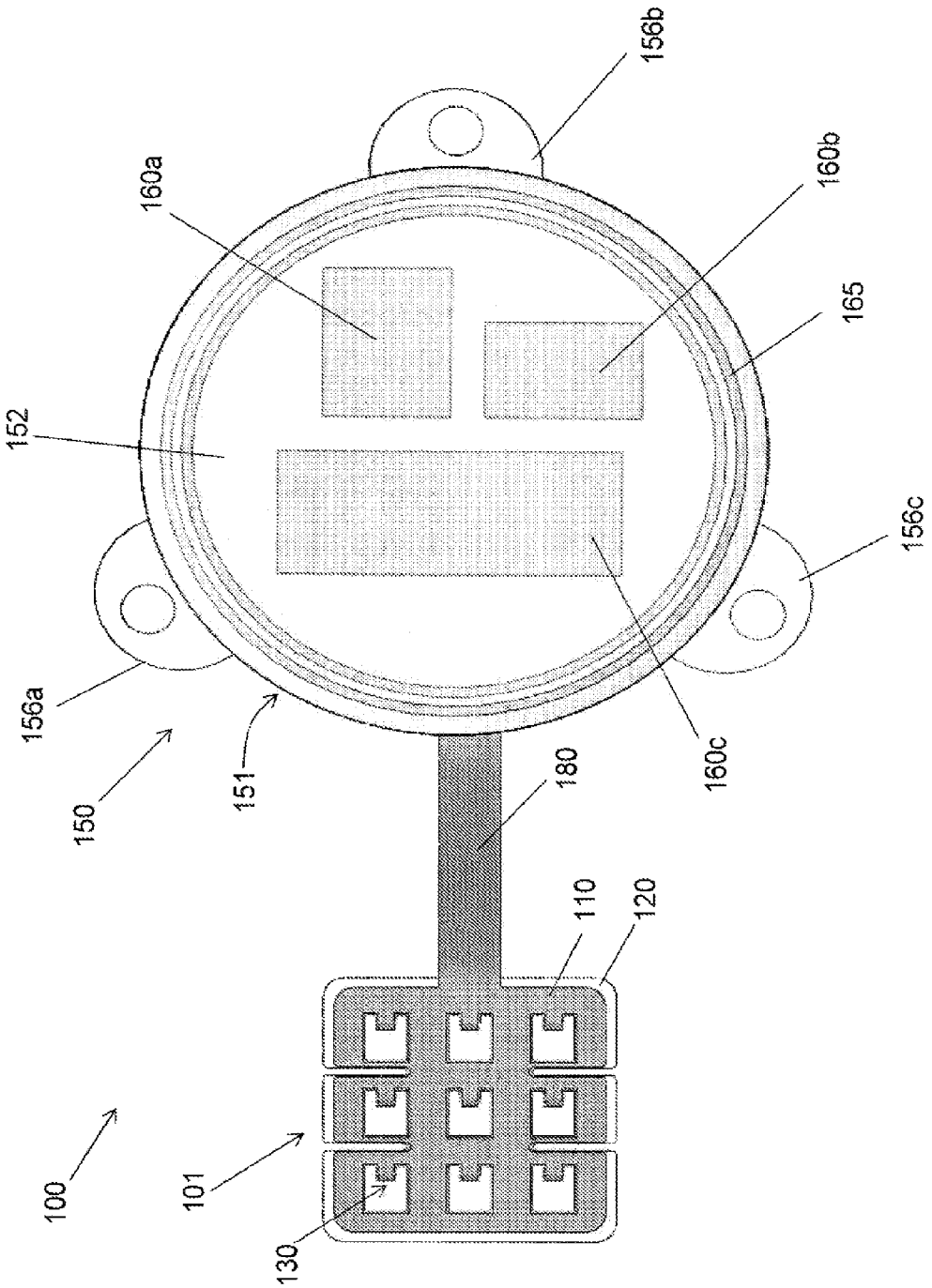
MICROELECTRODE ELEMENT (na) 140na
MICROELECTRODE ELEMENT (nn) 140nn
CORTICAL DEPTH PROBE (a) 130a
CORTICAL DEPTH PROBE (n) 130n
NEUROLOGICAL SURFACE PROBE 101
EXTERNAL CONTROLLER 170
CONTROL CIRCUITRY 160
100

FIG. 4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156c
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101
130

FIG. 5A

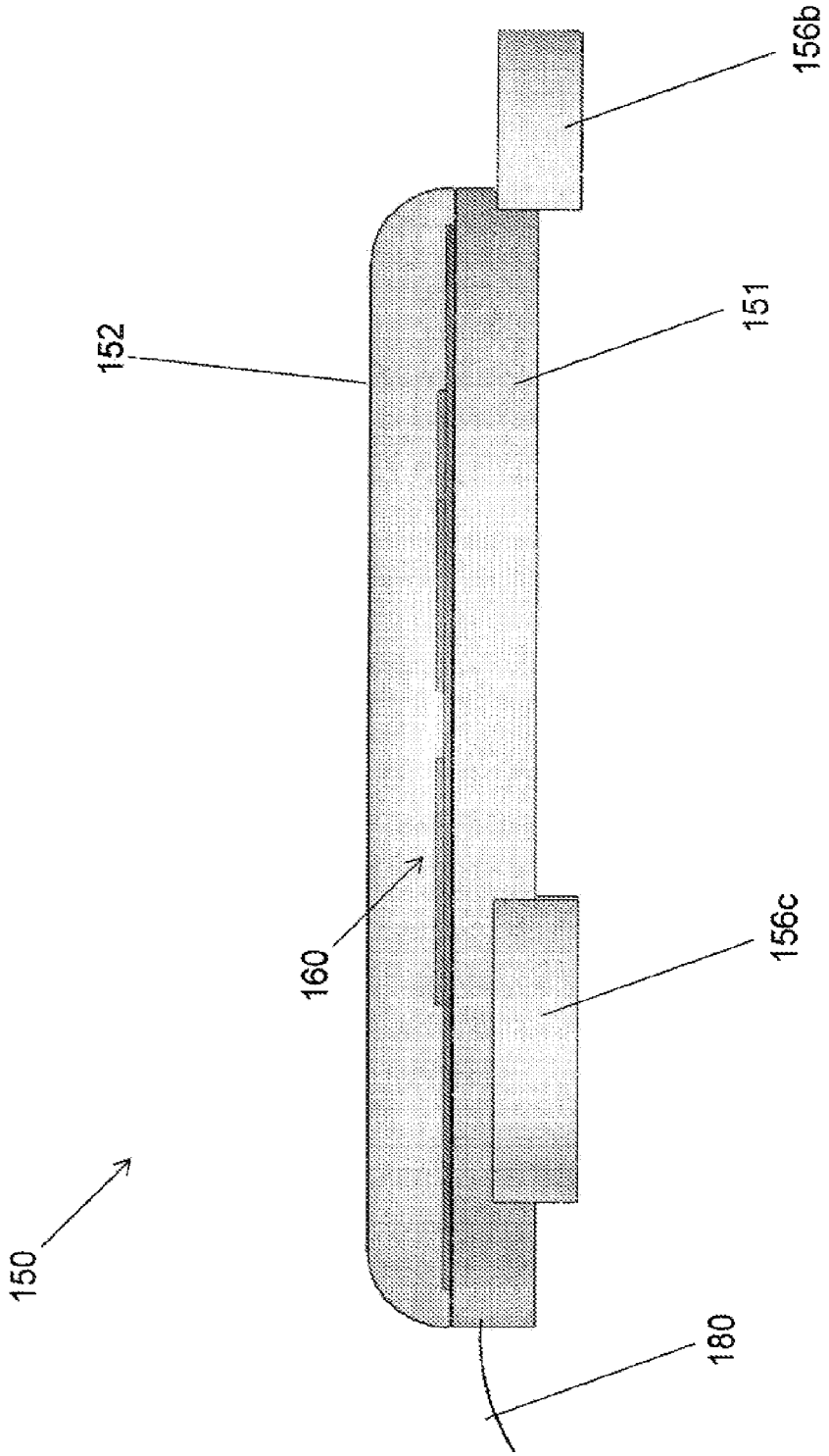
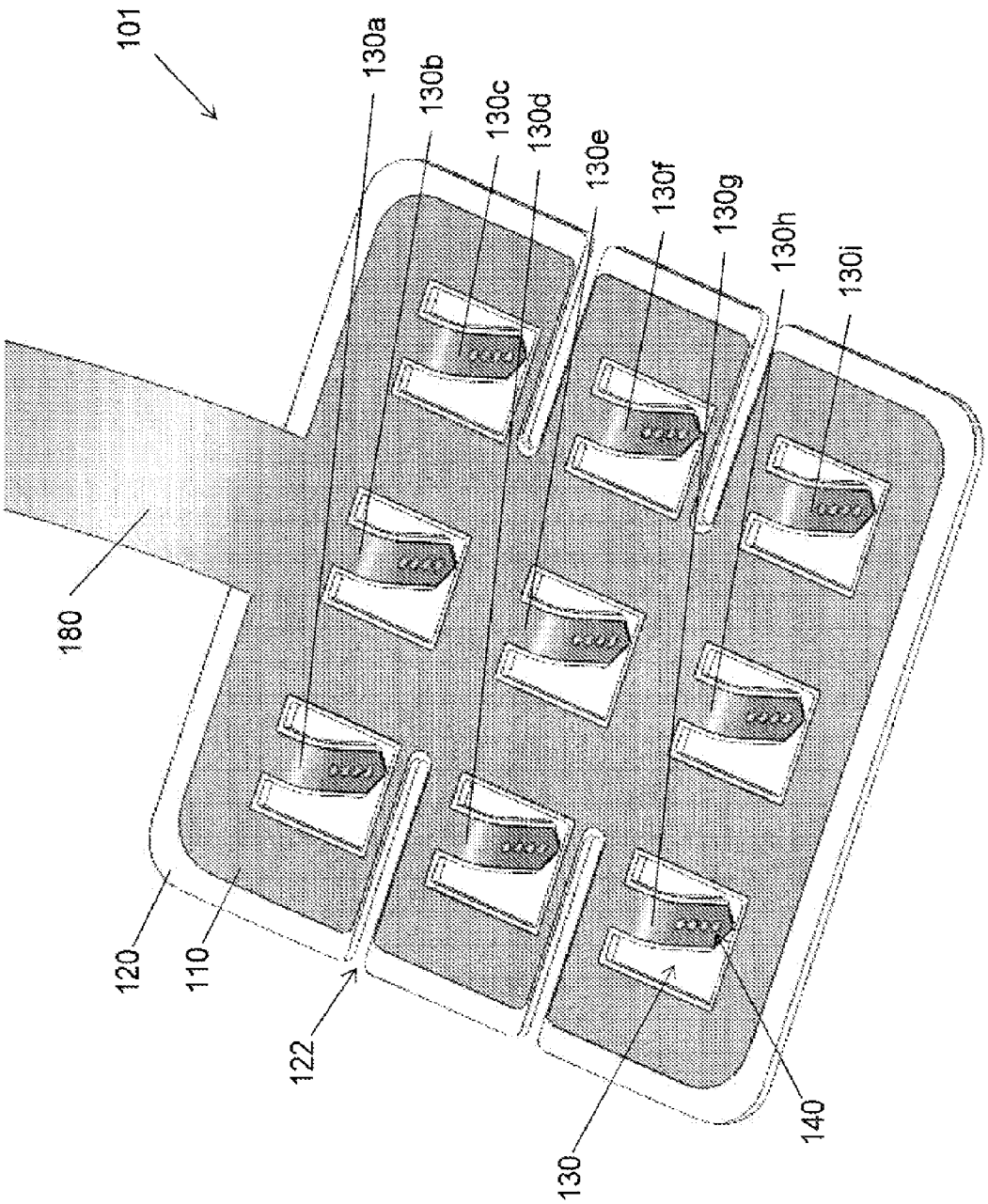


FIG. 5B


101
130a
130b
130c
130d
130e
130f
130g
130h
130i
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120
110
122
130
140

FIG. 6A

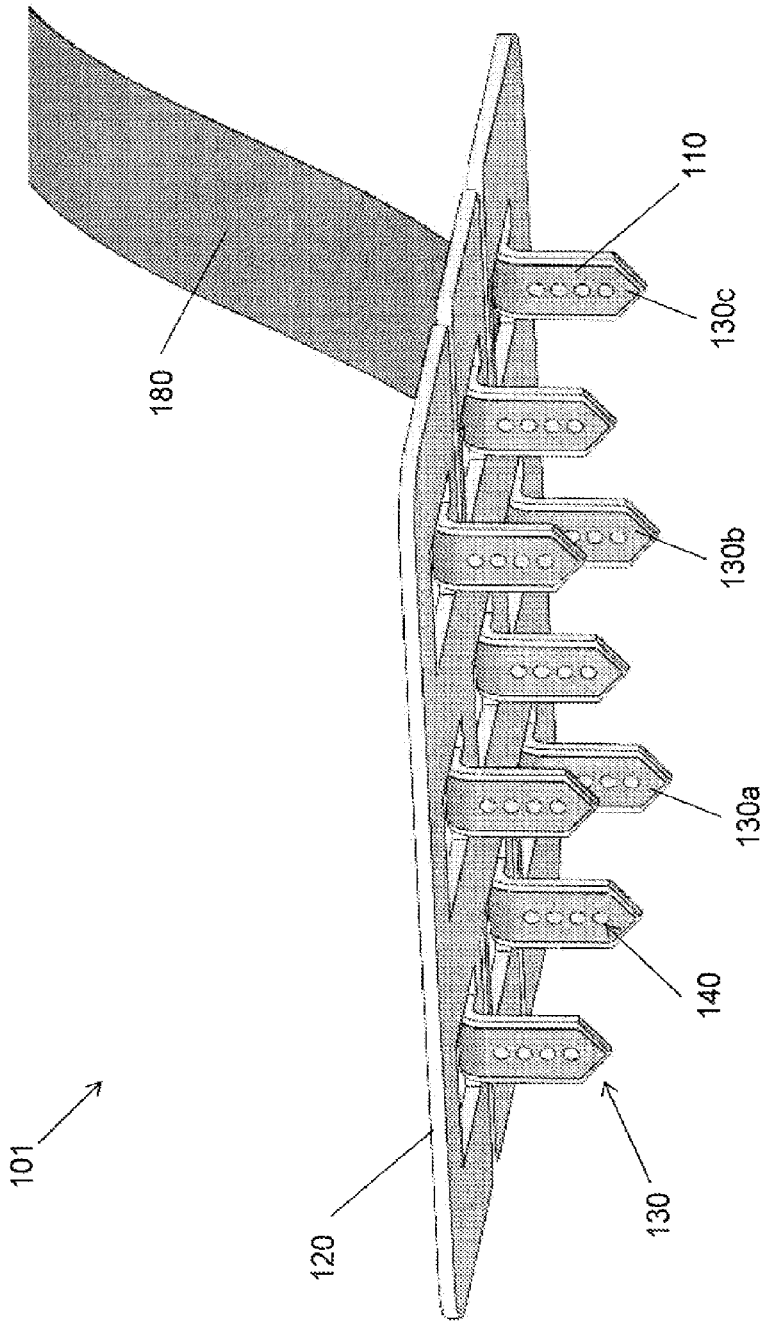

FIG. 6B

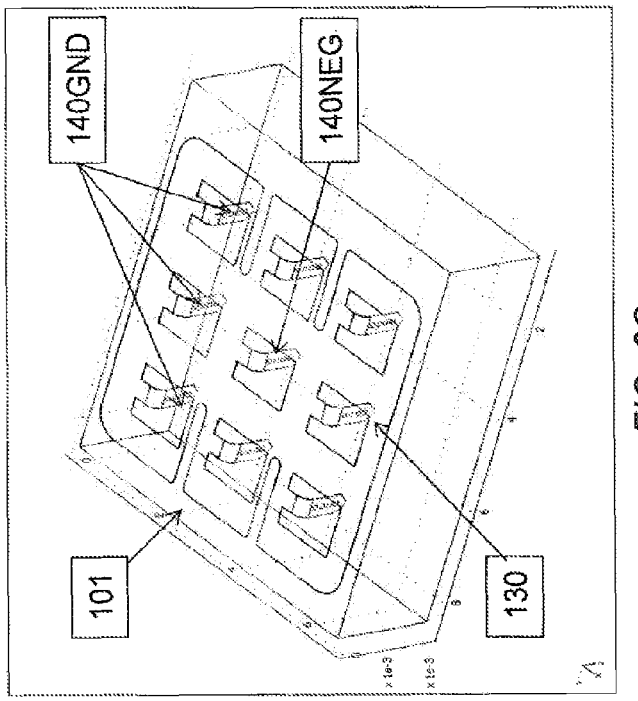

FIG. 6C

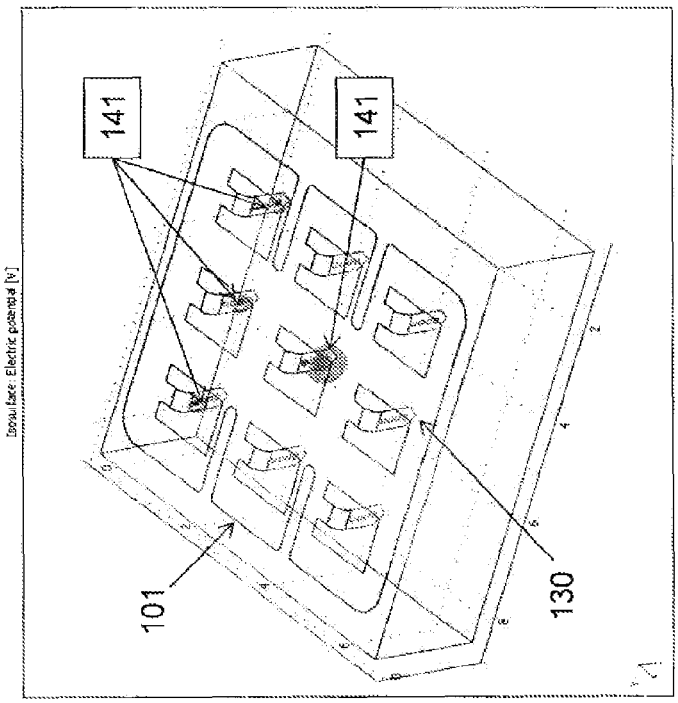

FIG. 6D

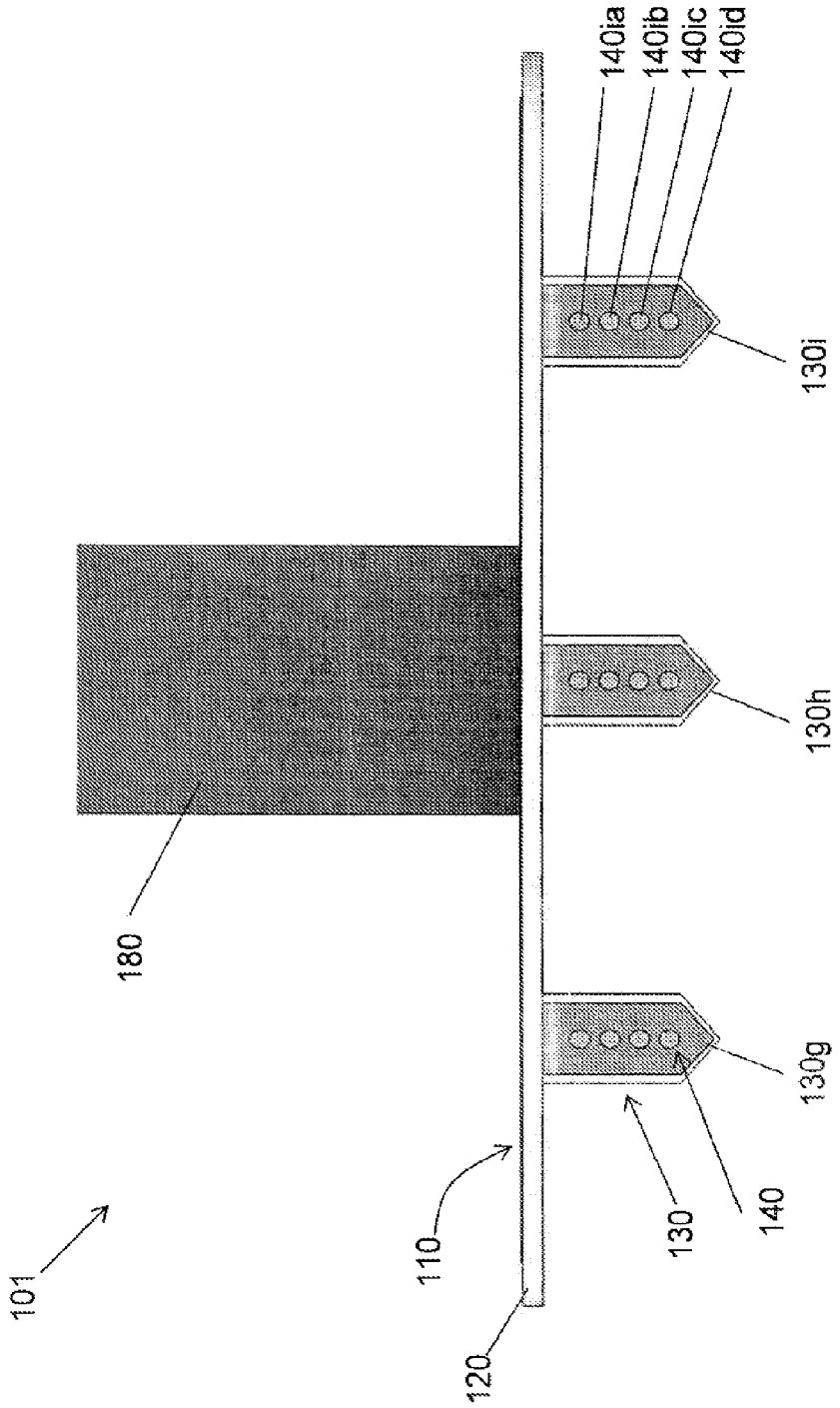
140ia
140ib
140ic
140id
130i
130h
130g
180
101
110
120
130
140

FIG. 7A

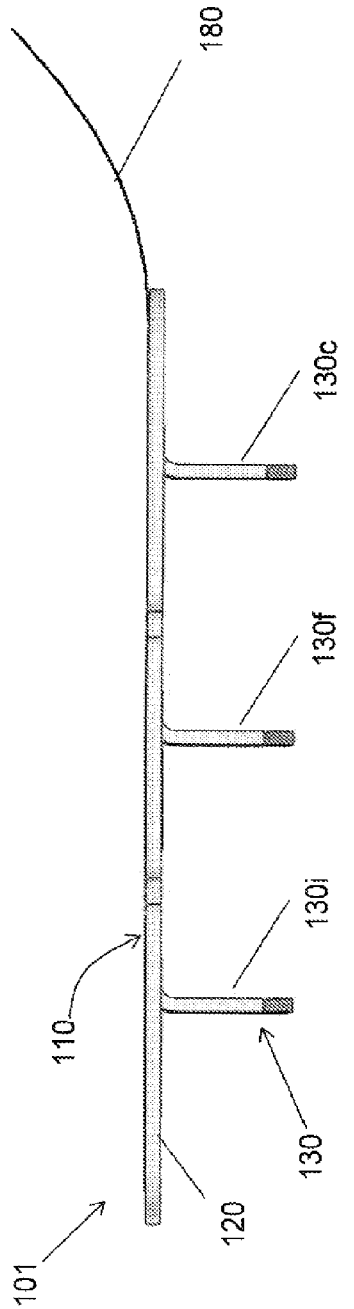

FIG. 7B

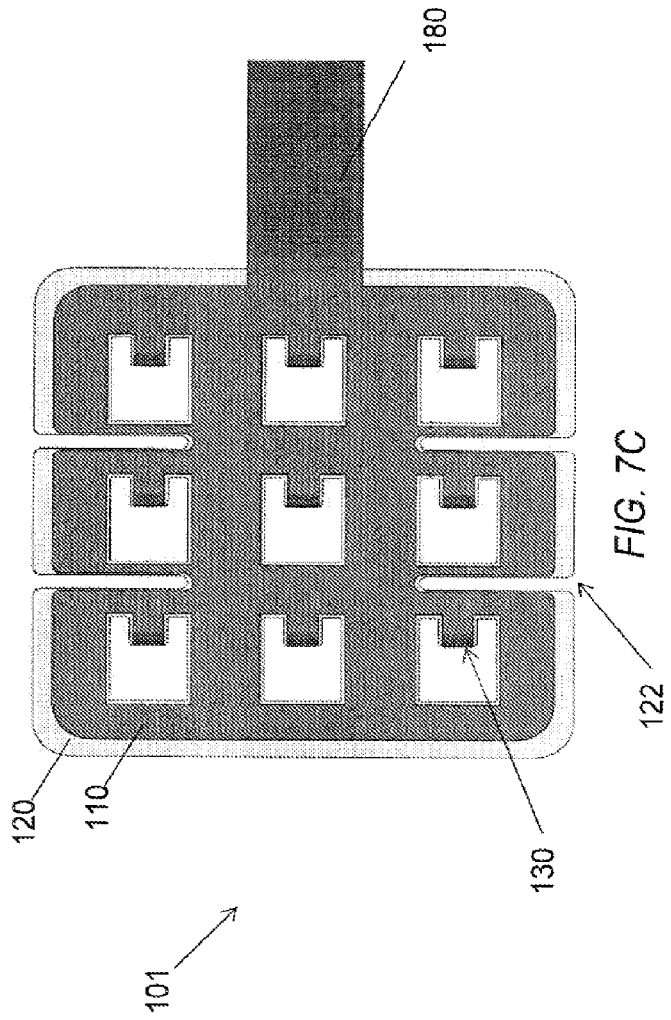

FIG. 7C

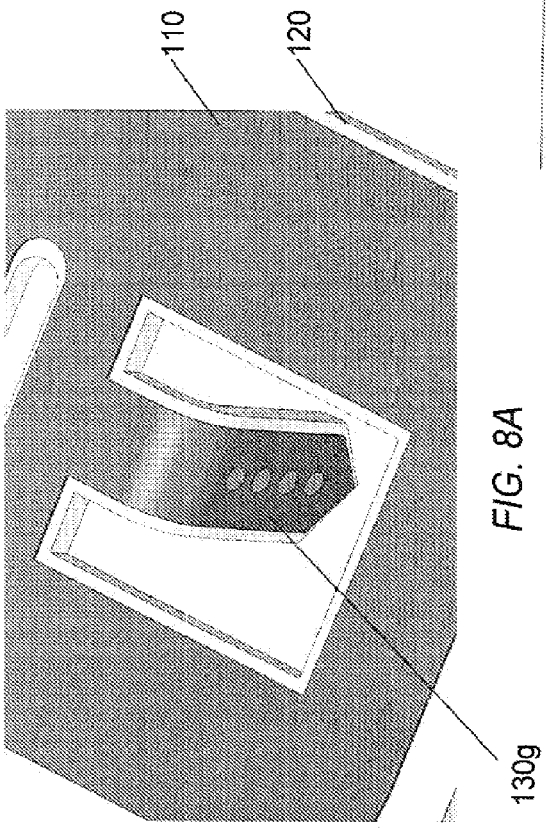

FIG. 8A

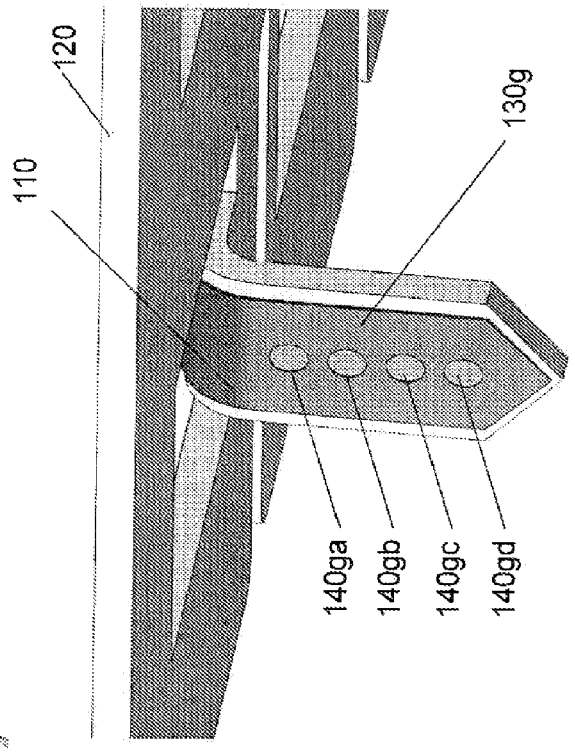

FIG. 8B

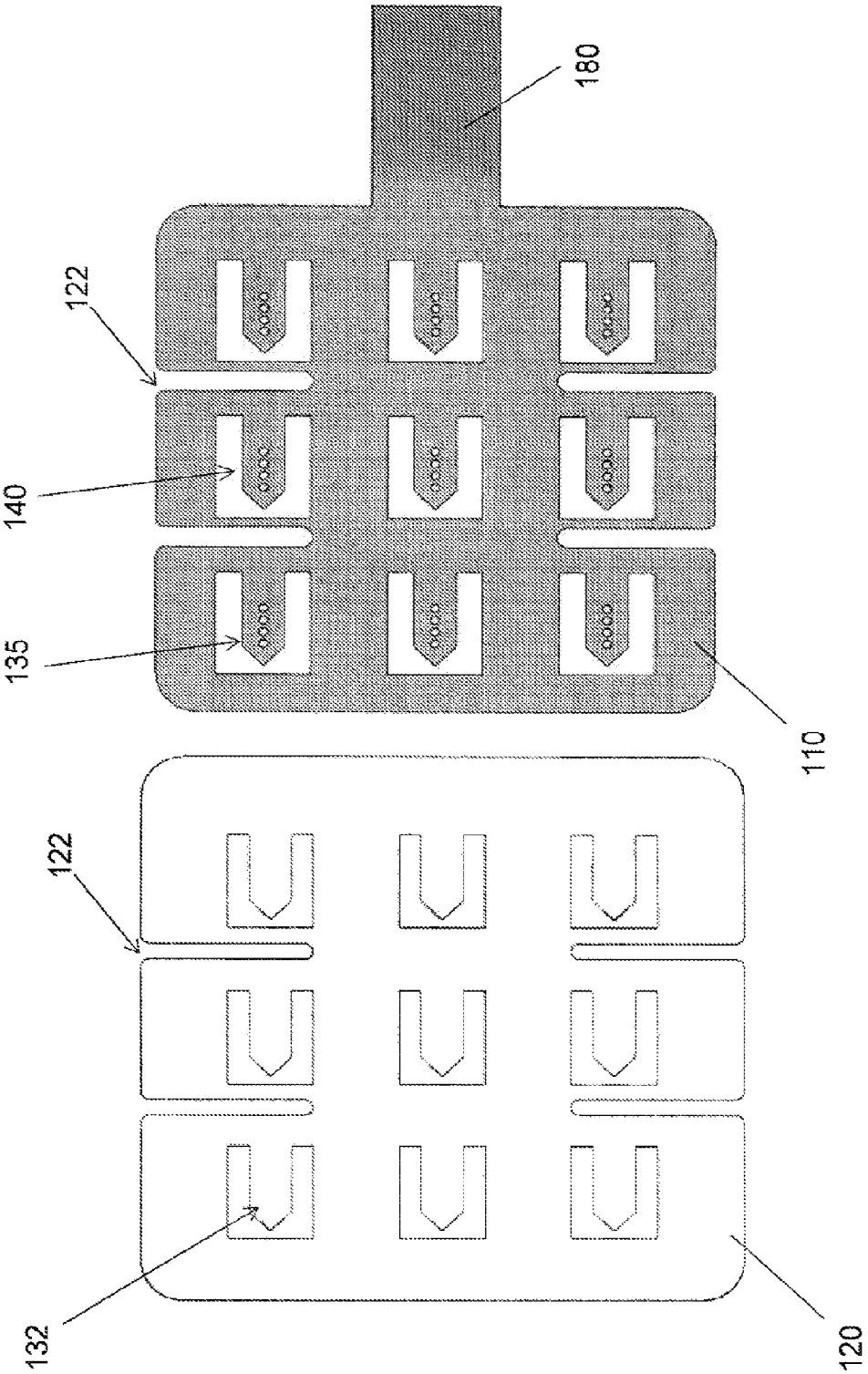

FIG. 9

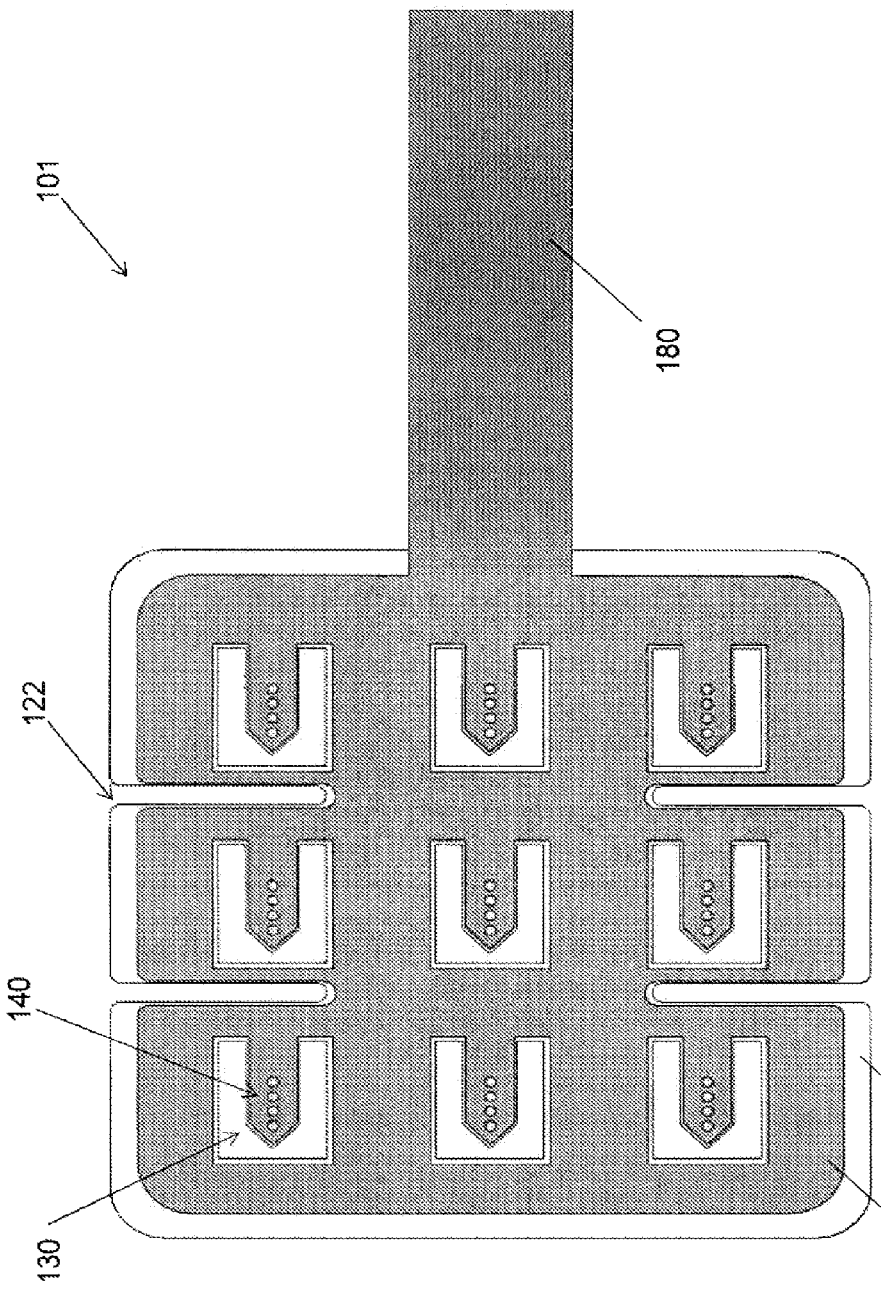

FIG. 10

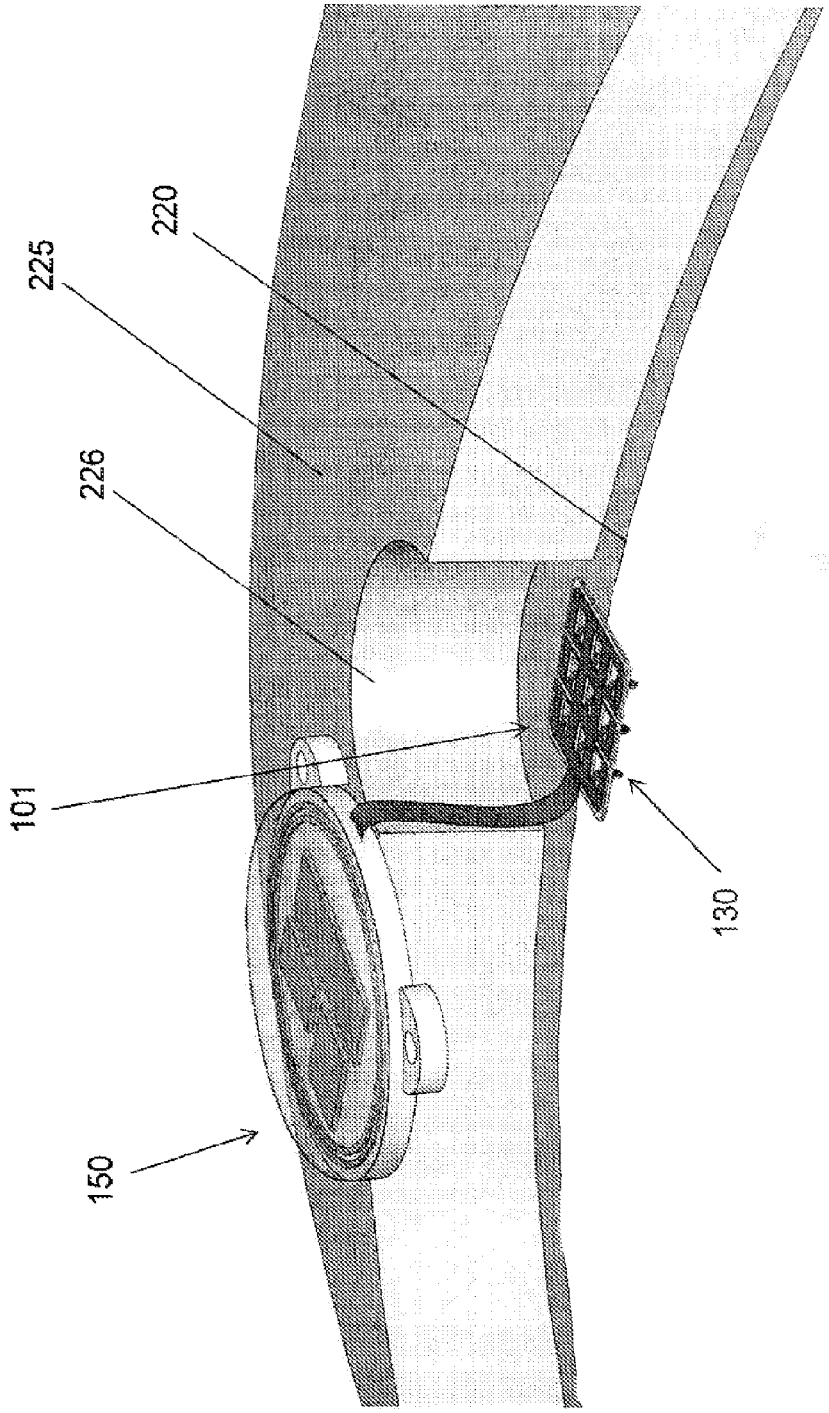

FIG. 11A

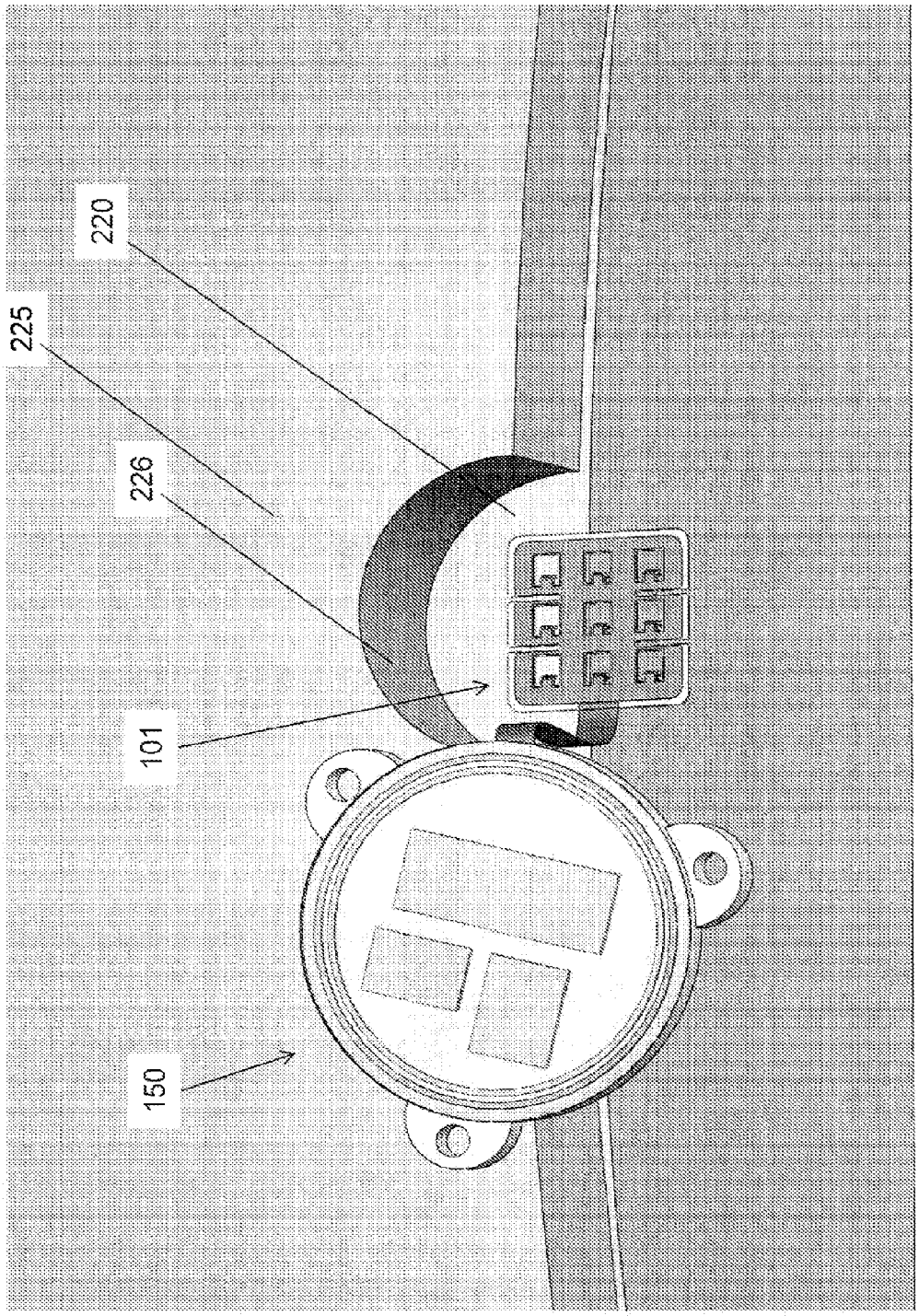

FIG. 11B

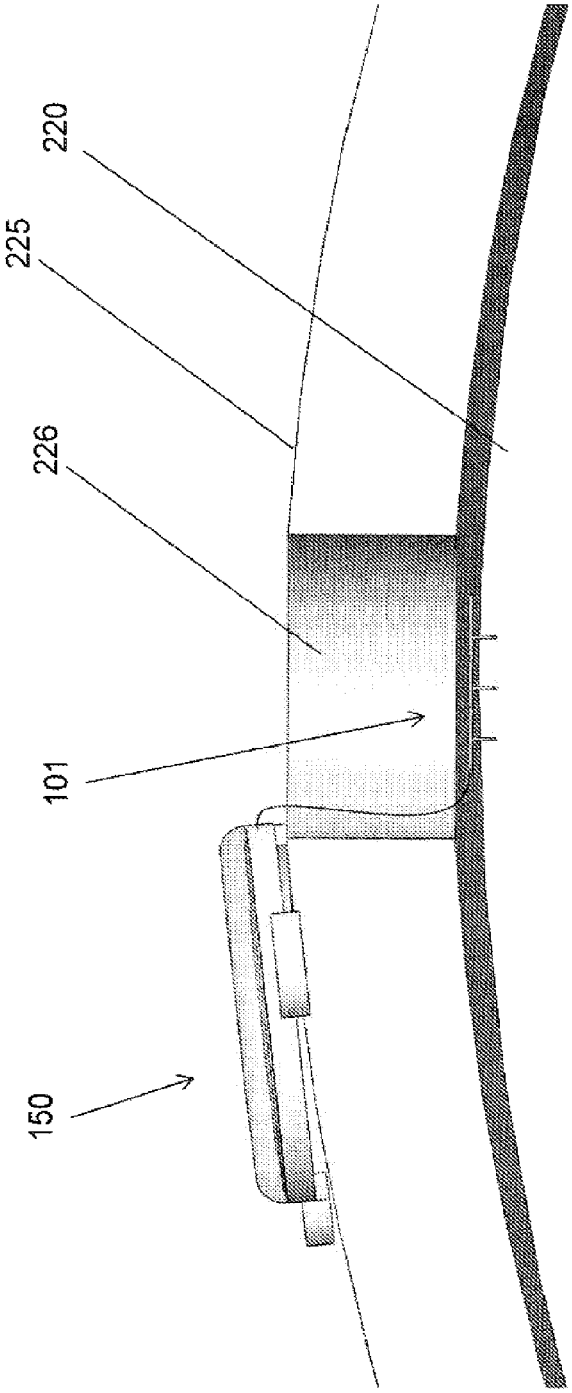

FIG. 11C

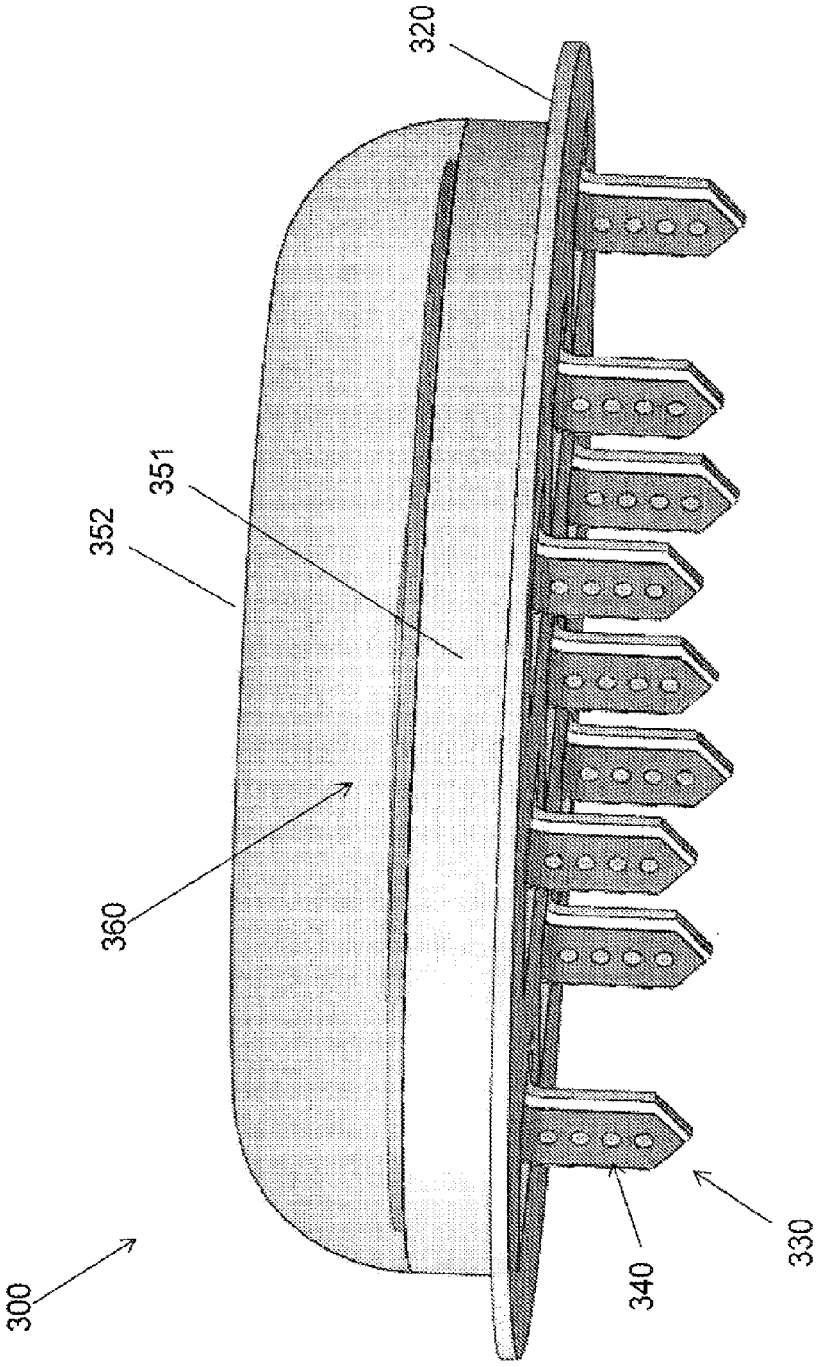

FIG. 12

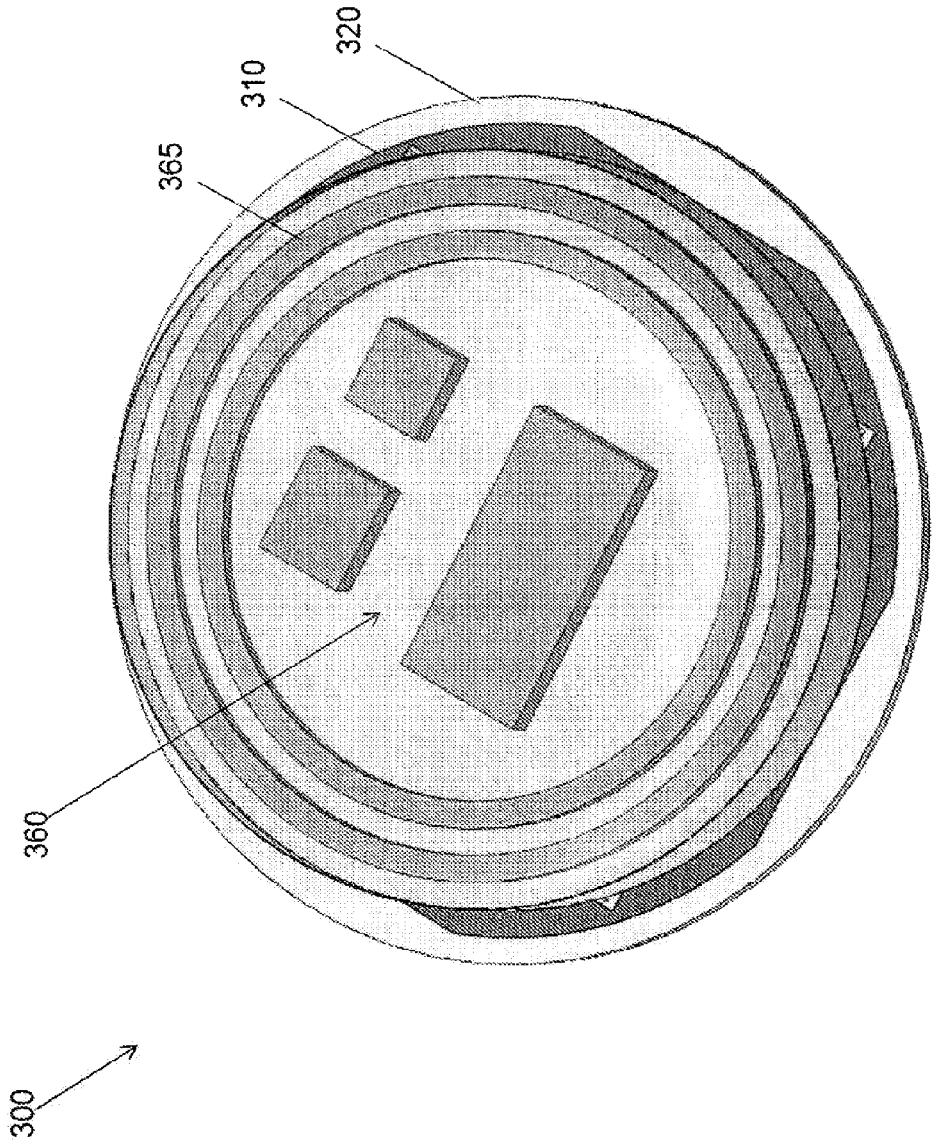

FIG. 13

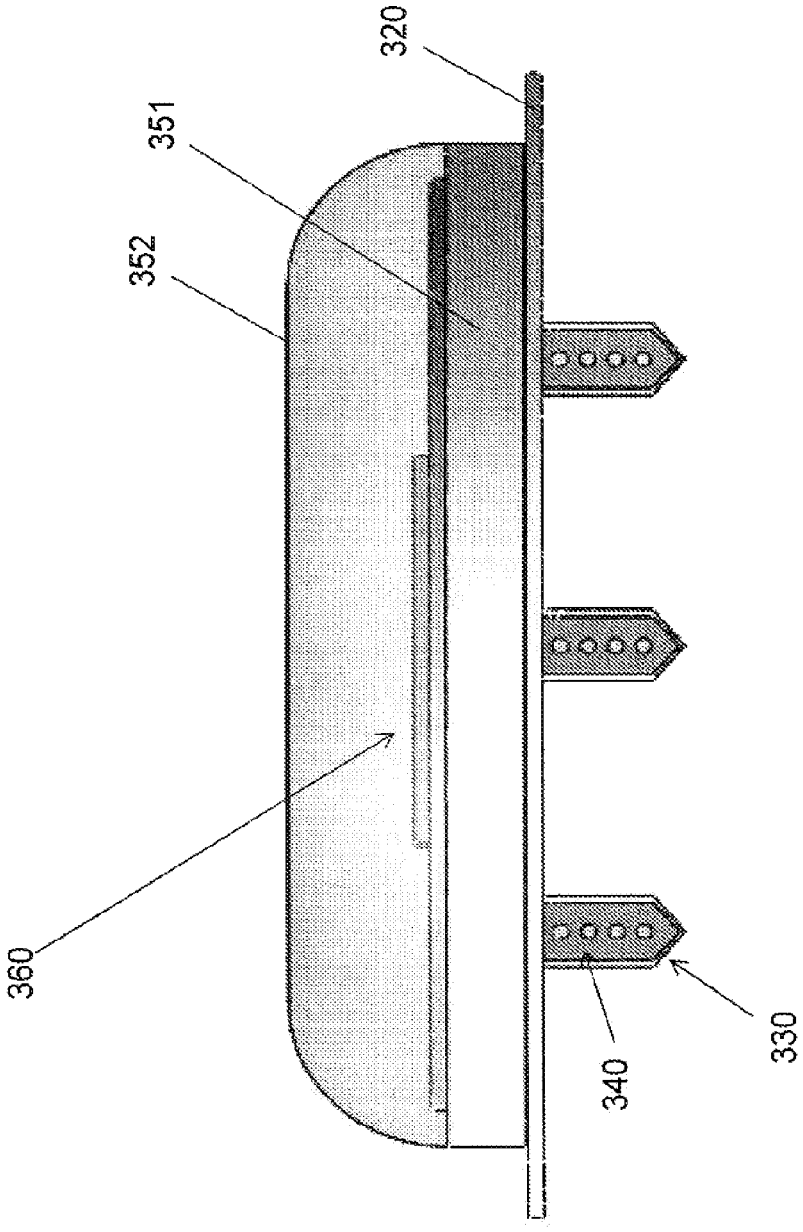

FIG. 14

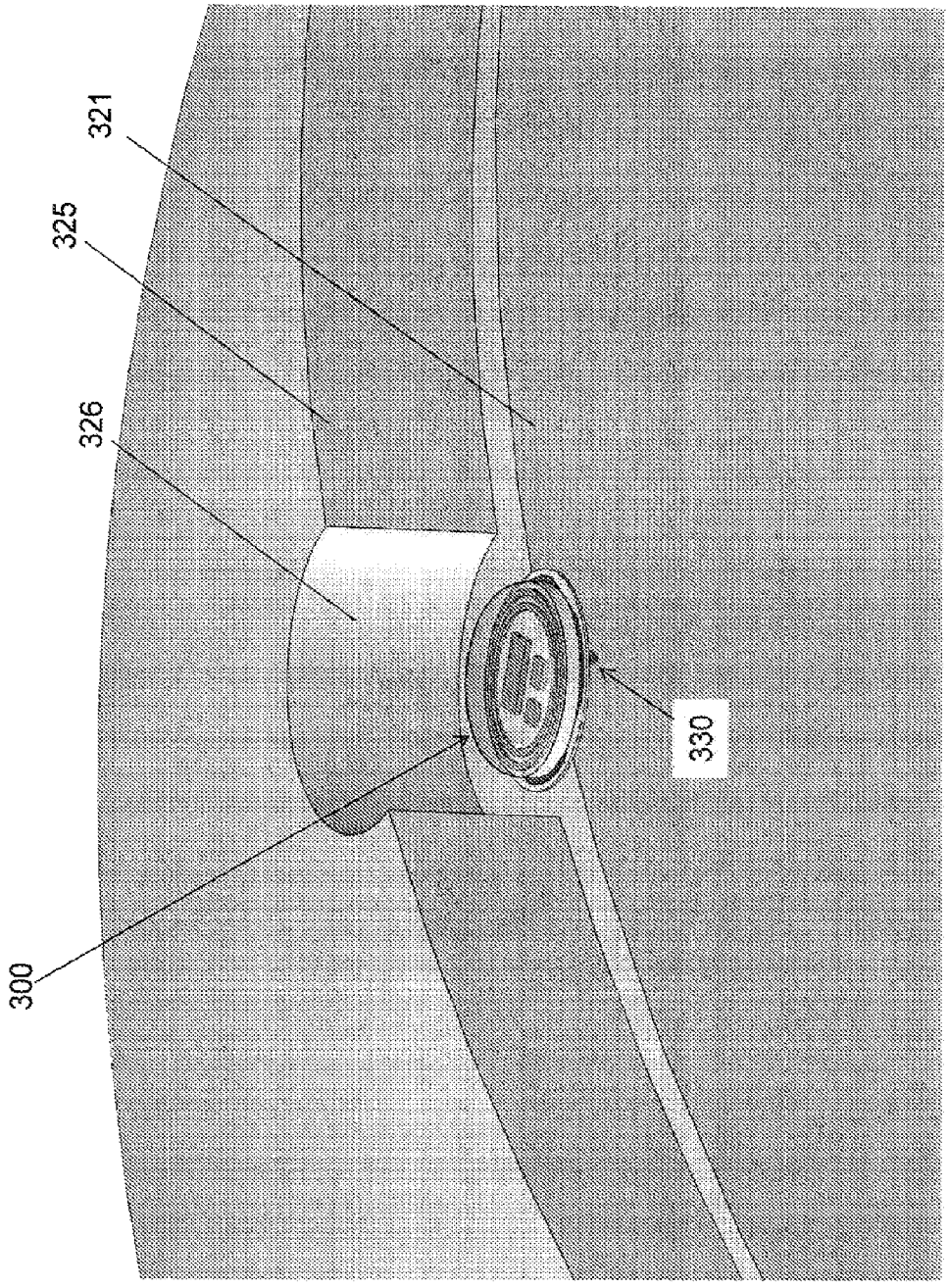

FIG. 15

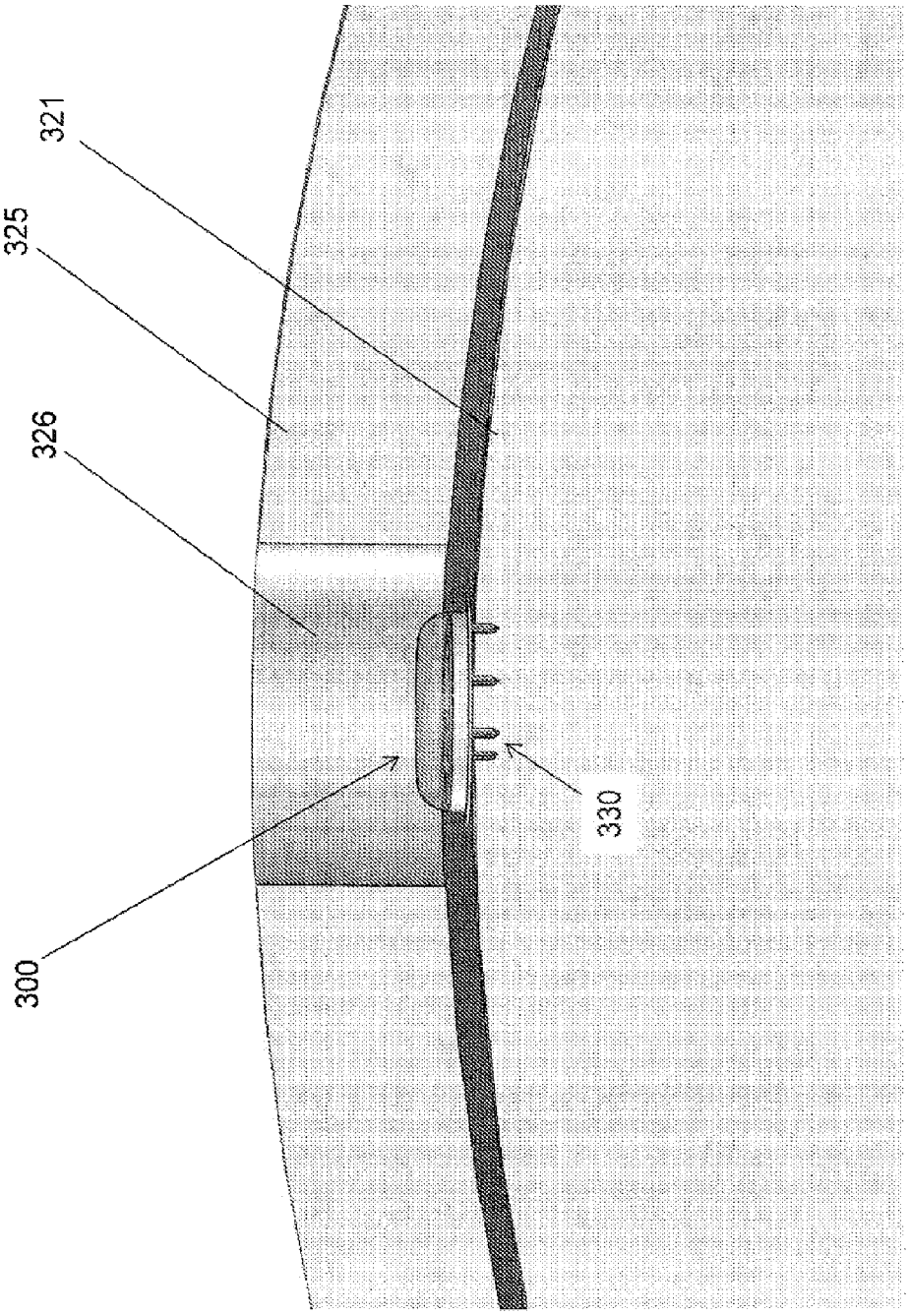

FIG. 16

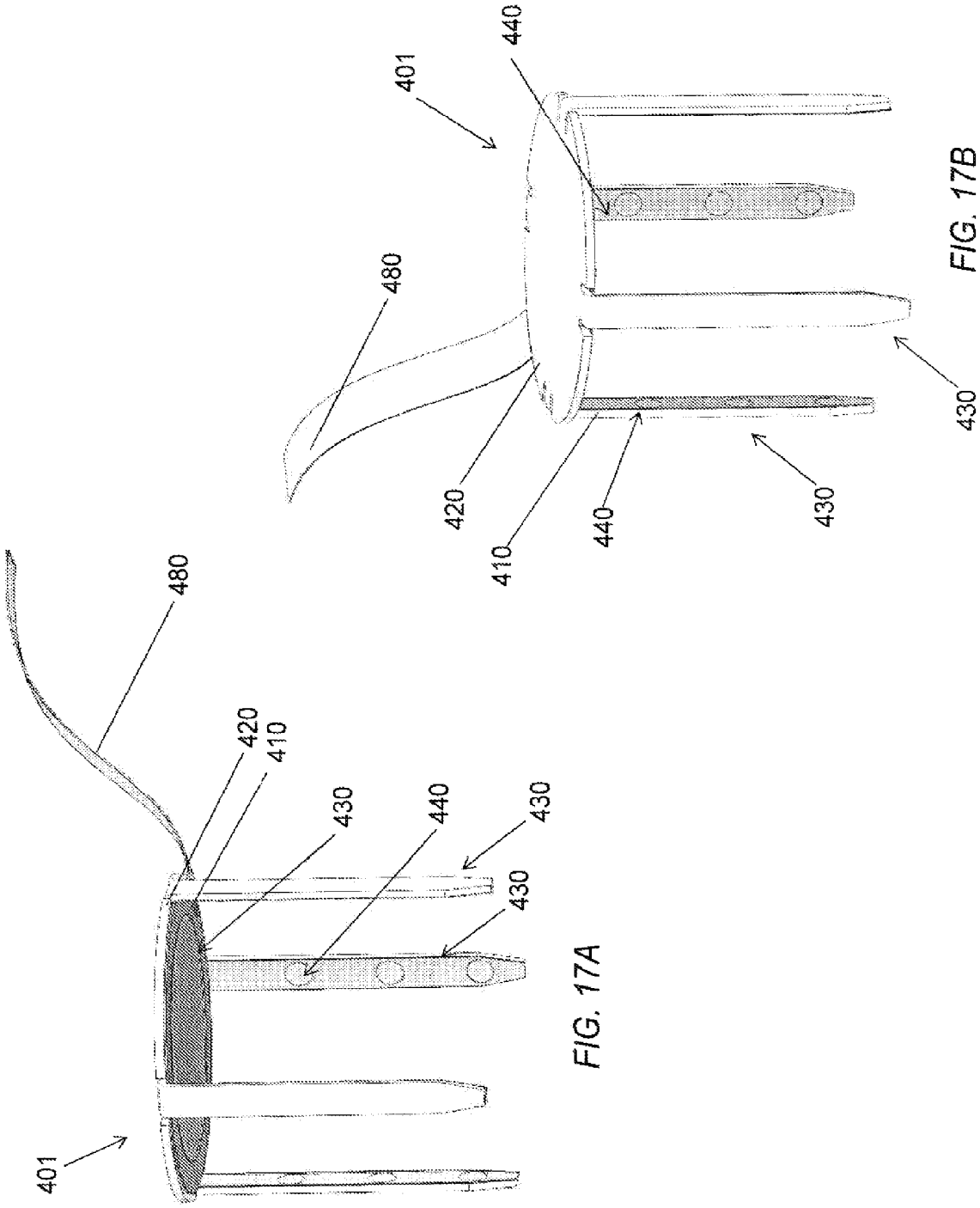

FIG. 17B

FIG. 17A

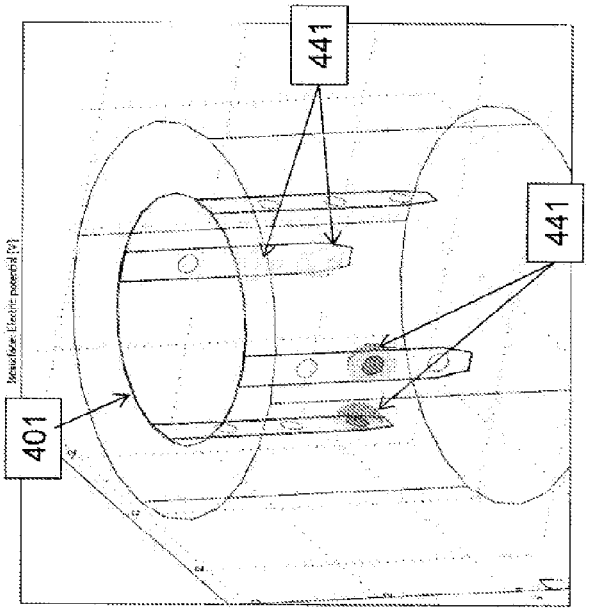

FIG. 17D

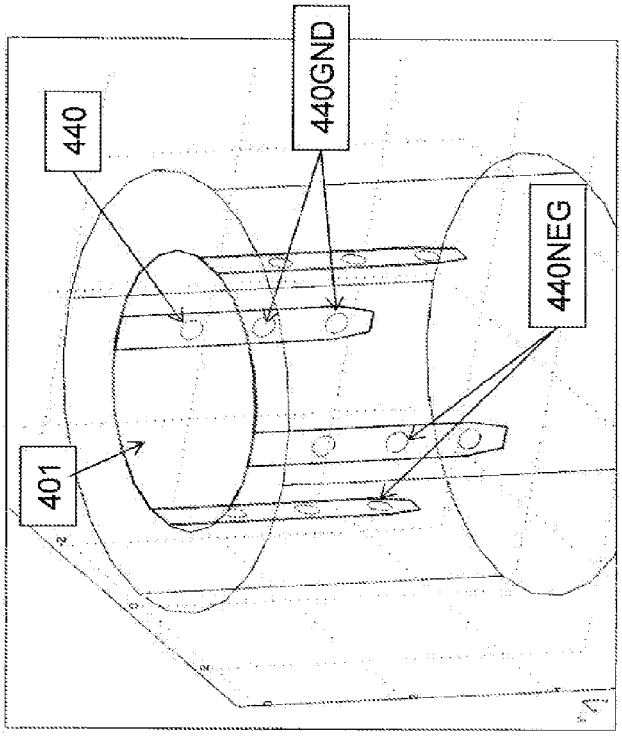

FIG. 17C

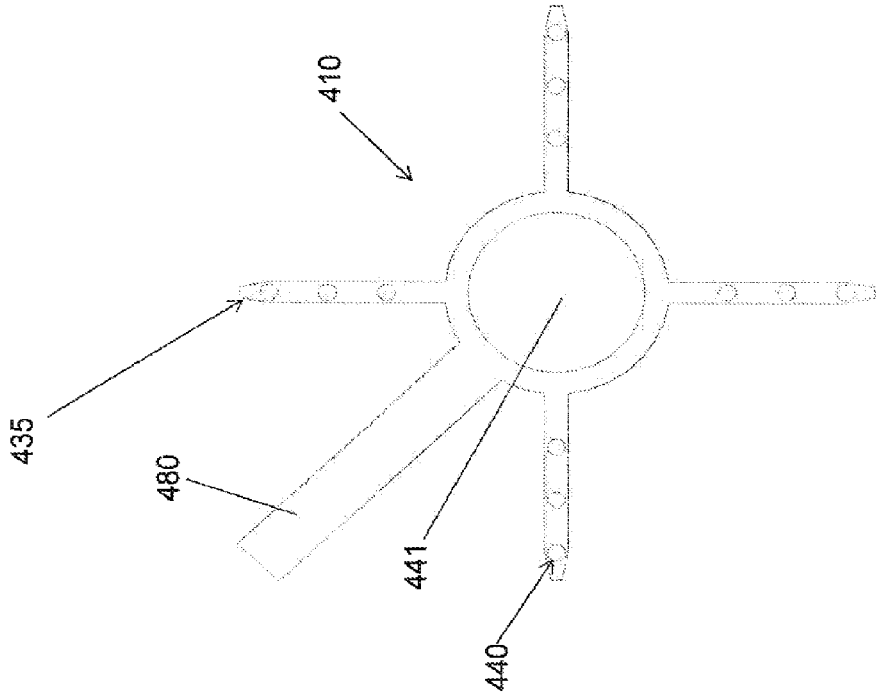

FIG. 18B

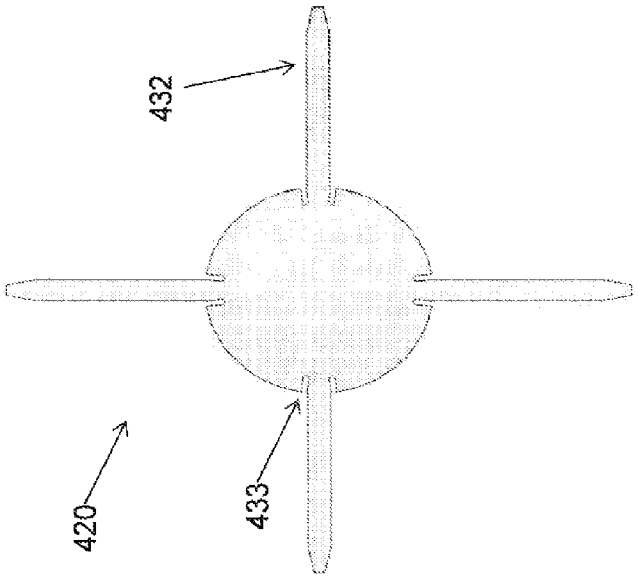

FIG. 18A

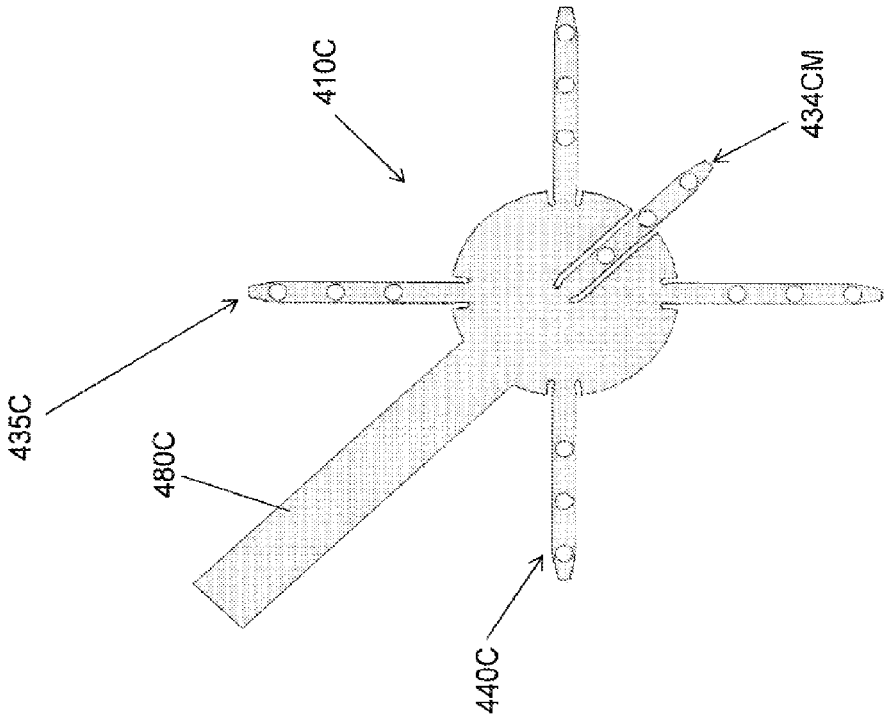

FIG. 18D

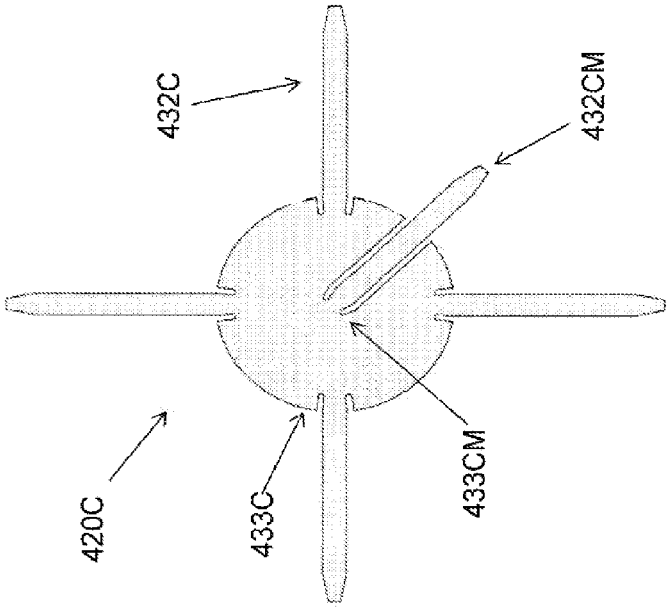

FIG. 18C

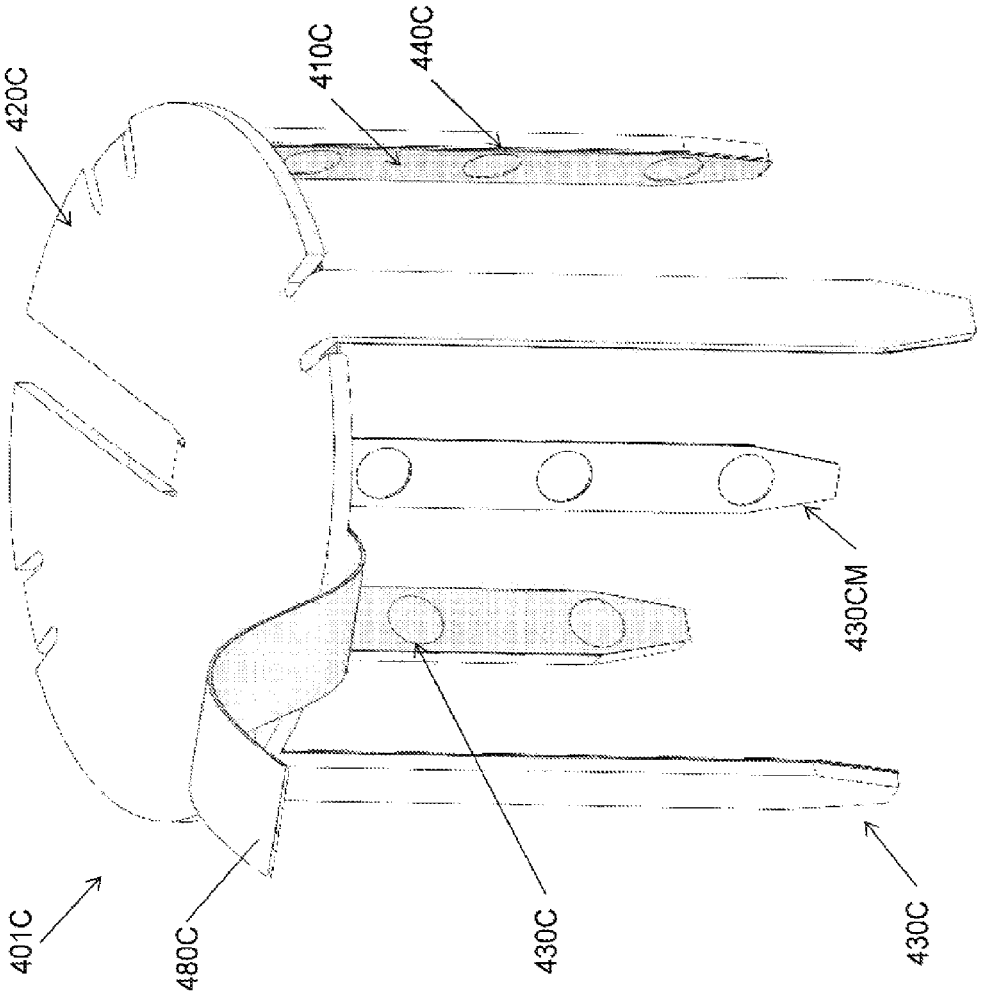

FIG. 18E

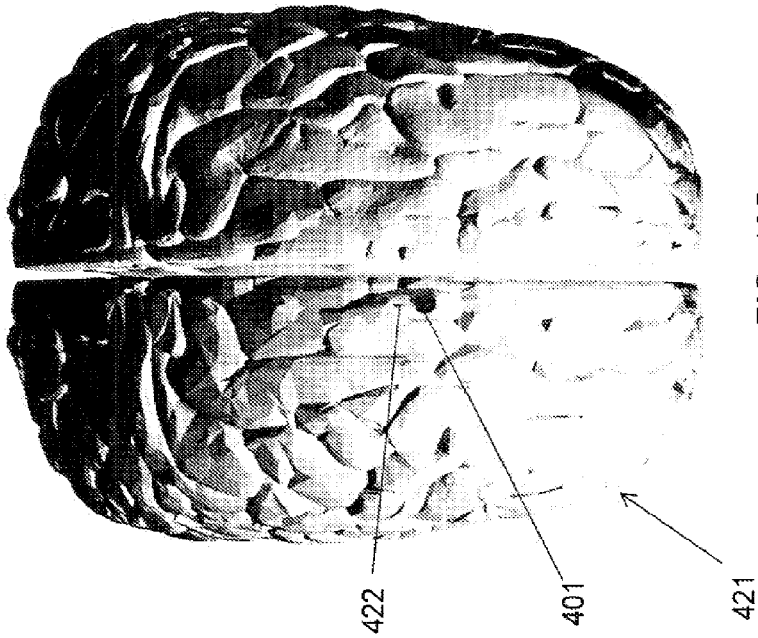

FIG. 19B

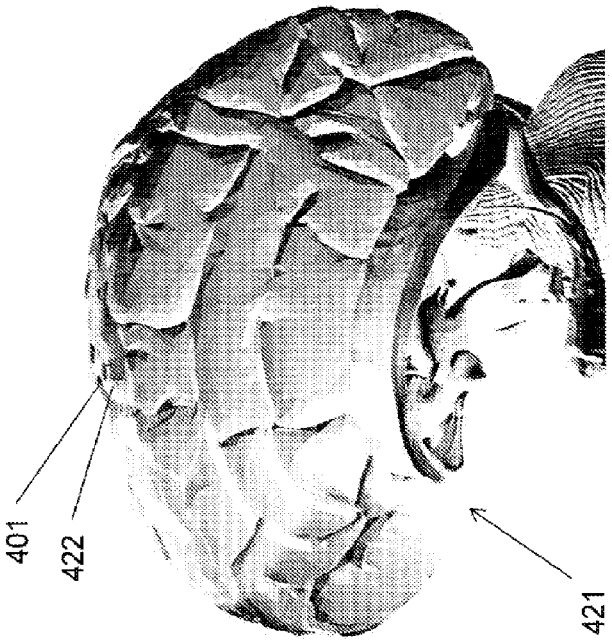

FIG. 19A

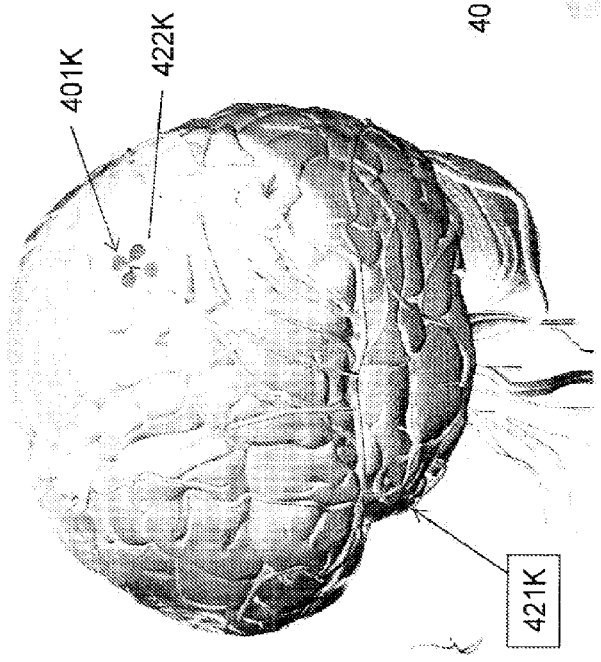

FIG. 20A

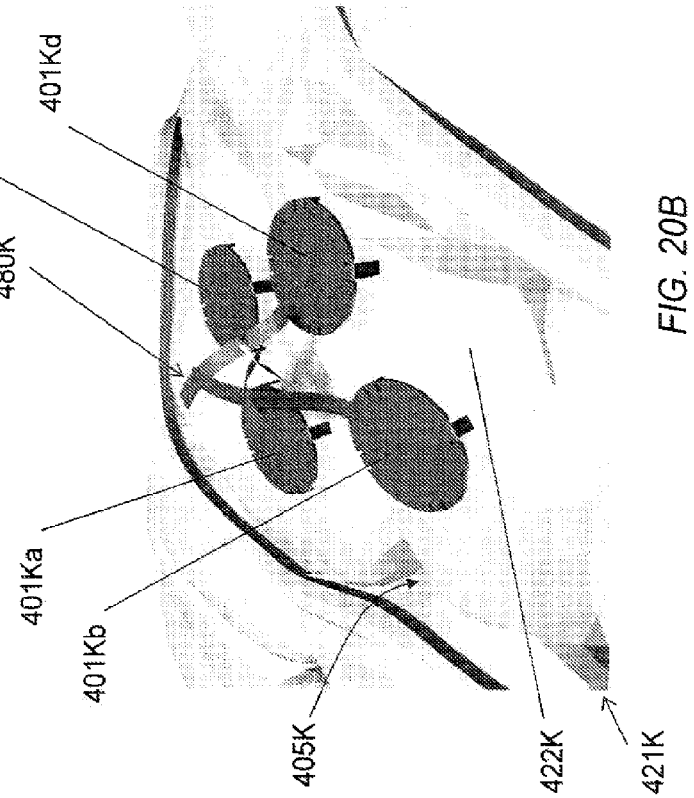

FIG. 20B

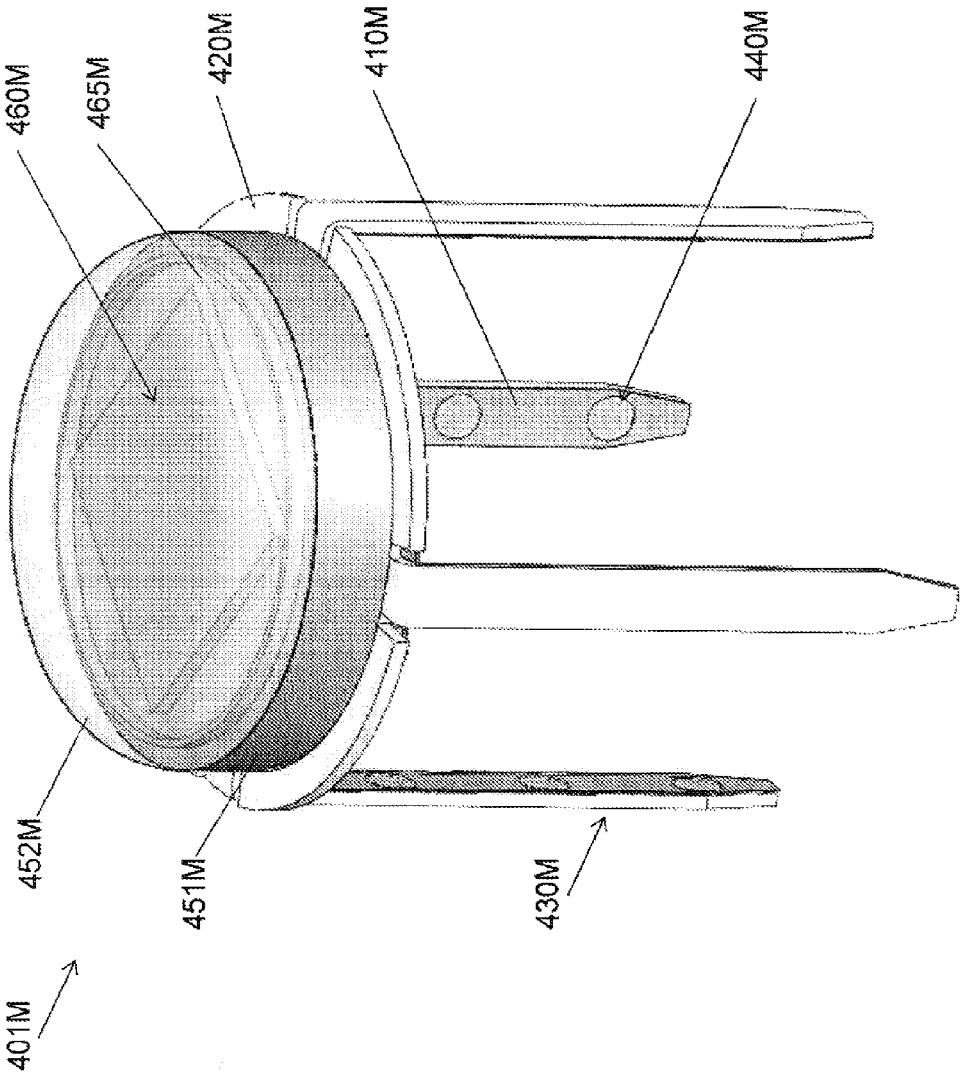

FIG. 21A

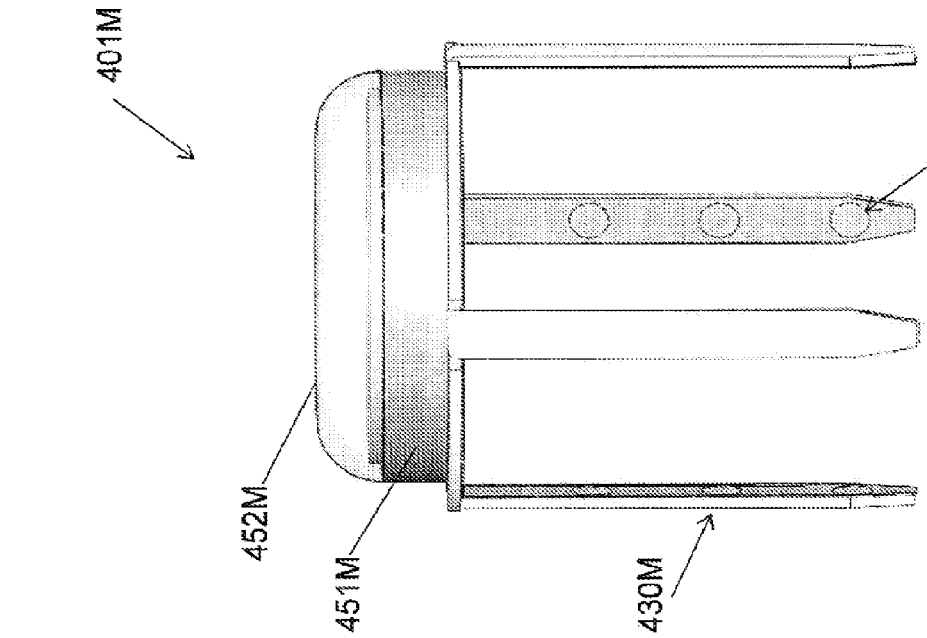

FIG. 21C

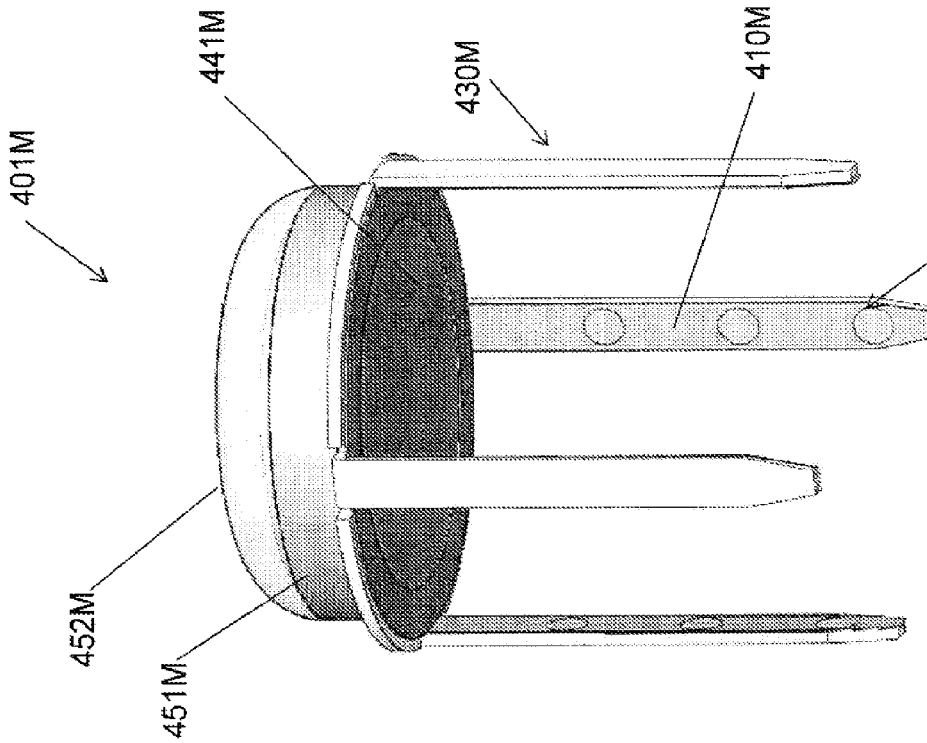

FIG. 21B

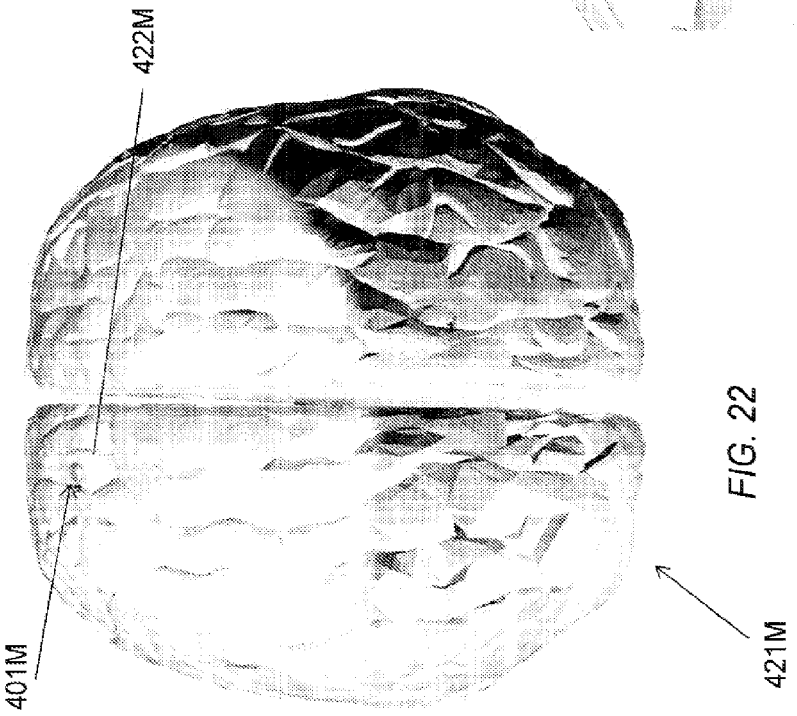

FIG. 22

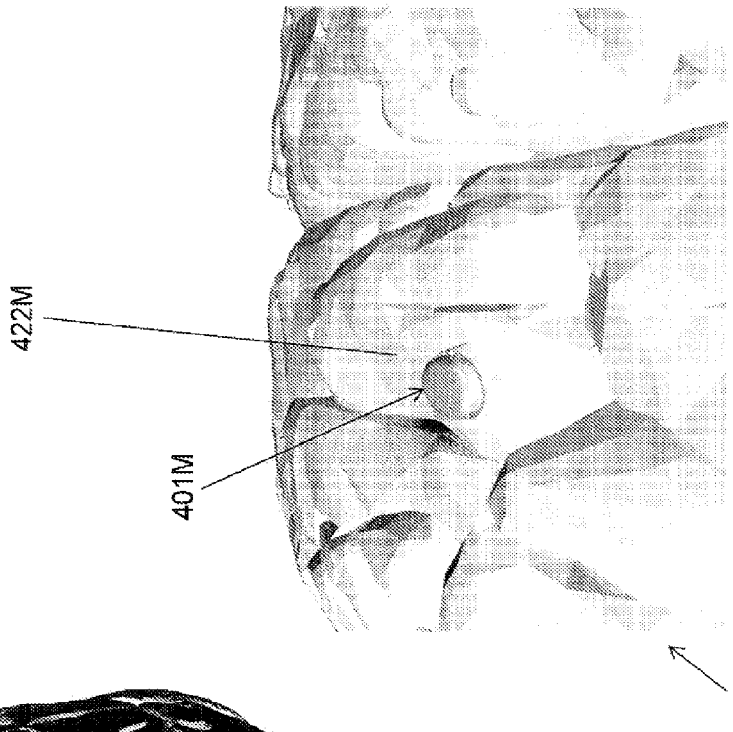

FIG. 23

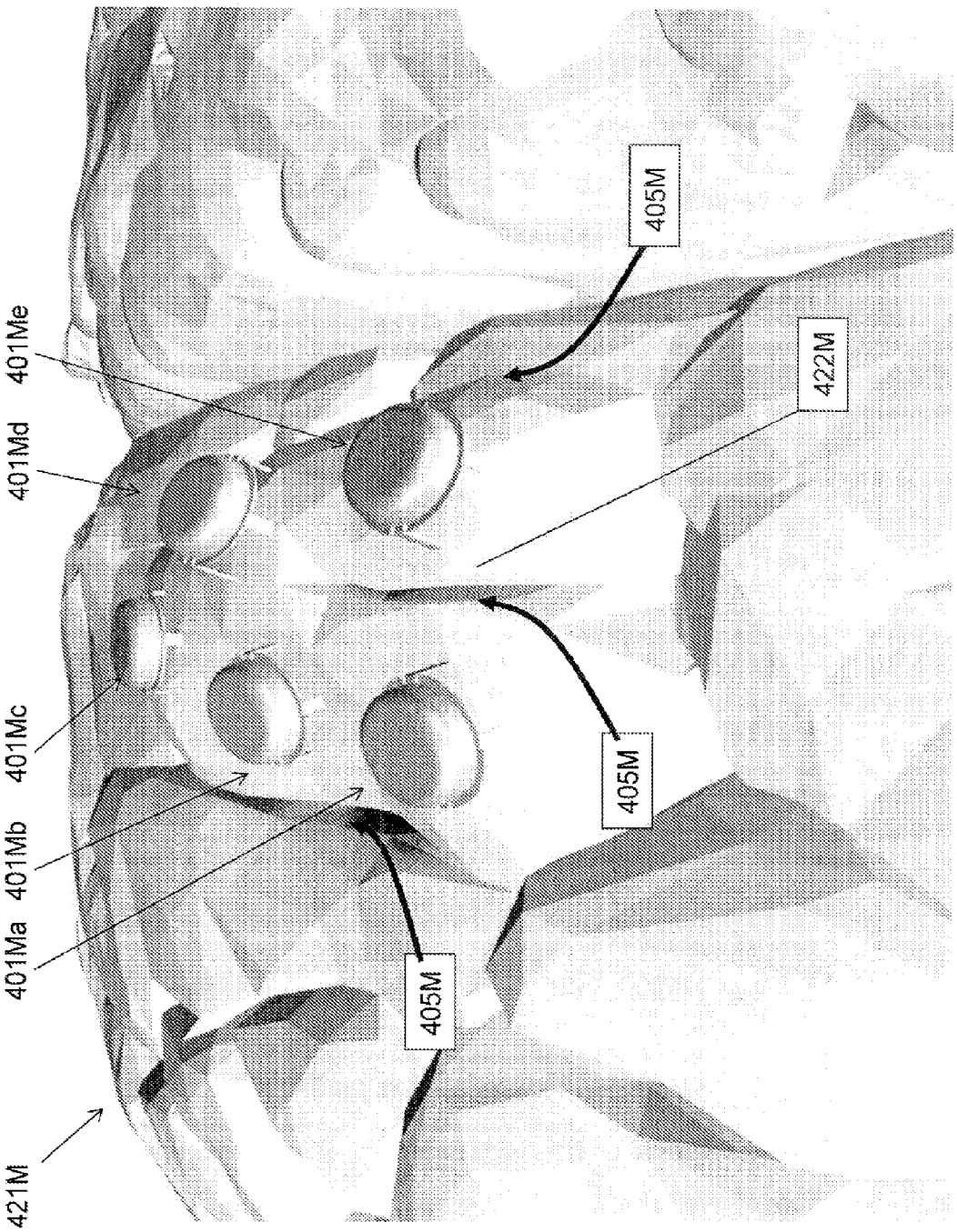

FIG. 24

FIG. 25A

FIG. 25B

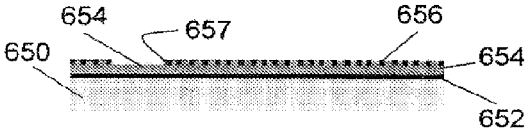

FIG. 25C

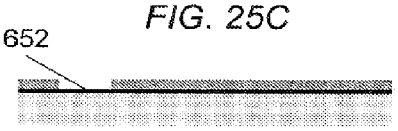

FIG. 25D

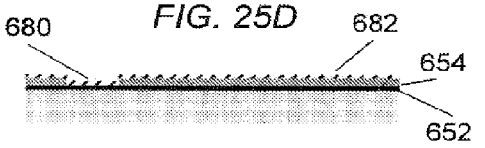

FIG. 25E

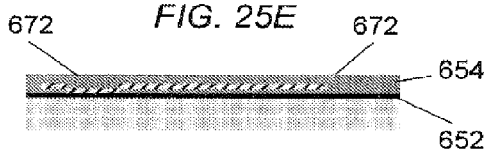

FIG. 25F

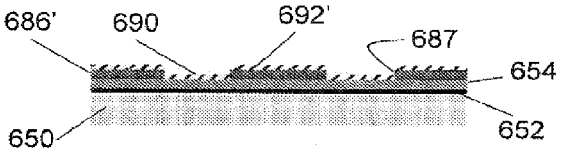

FIG. 25G

FIG. 25H

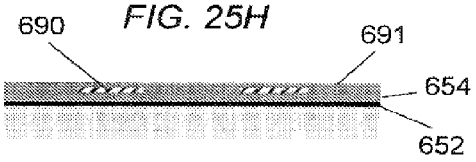

FIG. 25I

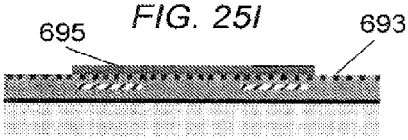

FIG. 25J

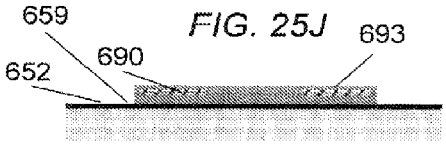

FIG. 25K

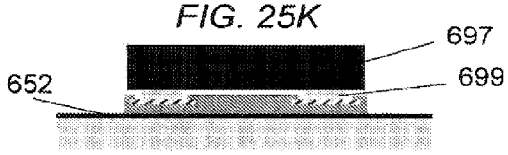

FIG. 25L

FIG. 25M

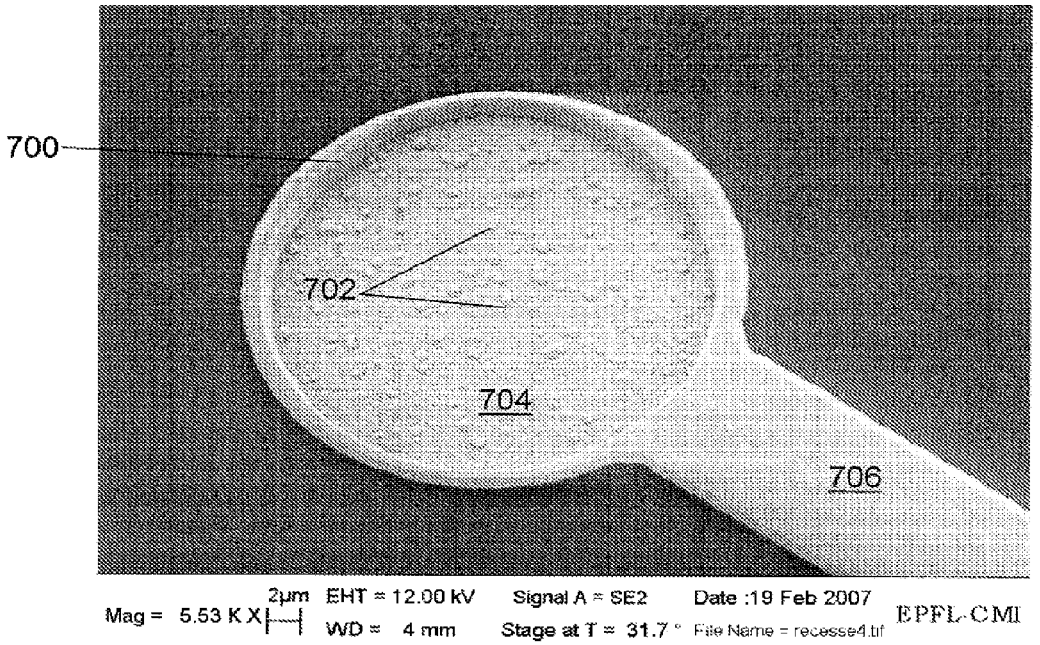
700
702
704
706
Mag = 5.53 K X
2µm
EHT = 12.00 kV
WD = 4 mm
Signal A = SE2
Stage at T = 31.7 °
Date :19 Feb 2007
File Name = recesse4.tif
EPFL-CMI

FIG. 26

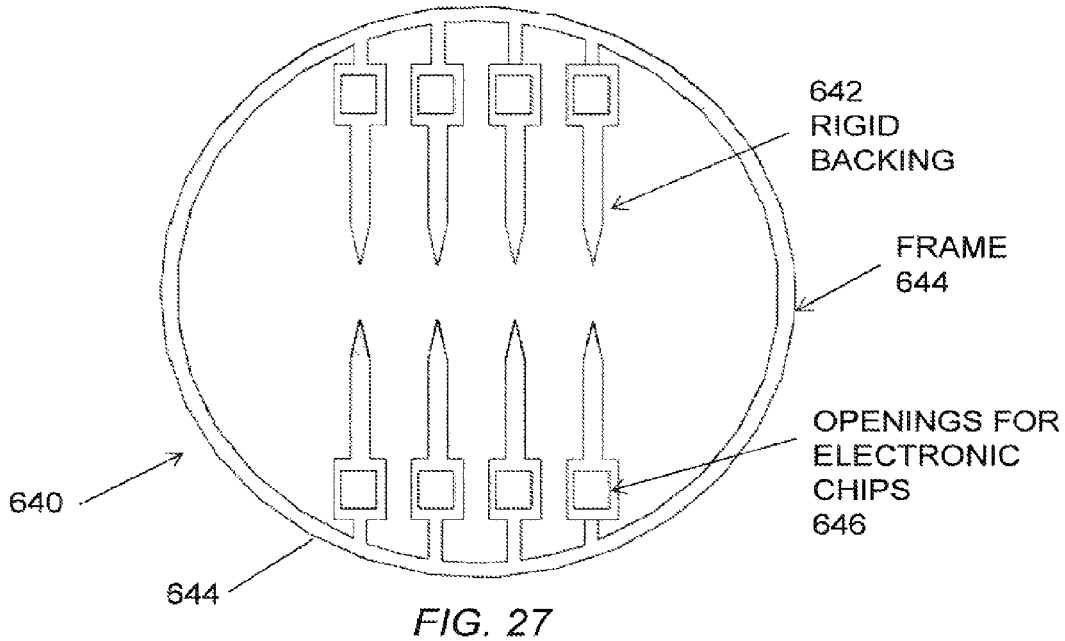
642
RIGID
BACKING
FRAME
644
OPENINGS FOR
ELECTRONIC
CHIPS
646
640
644

FIG. 27

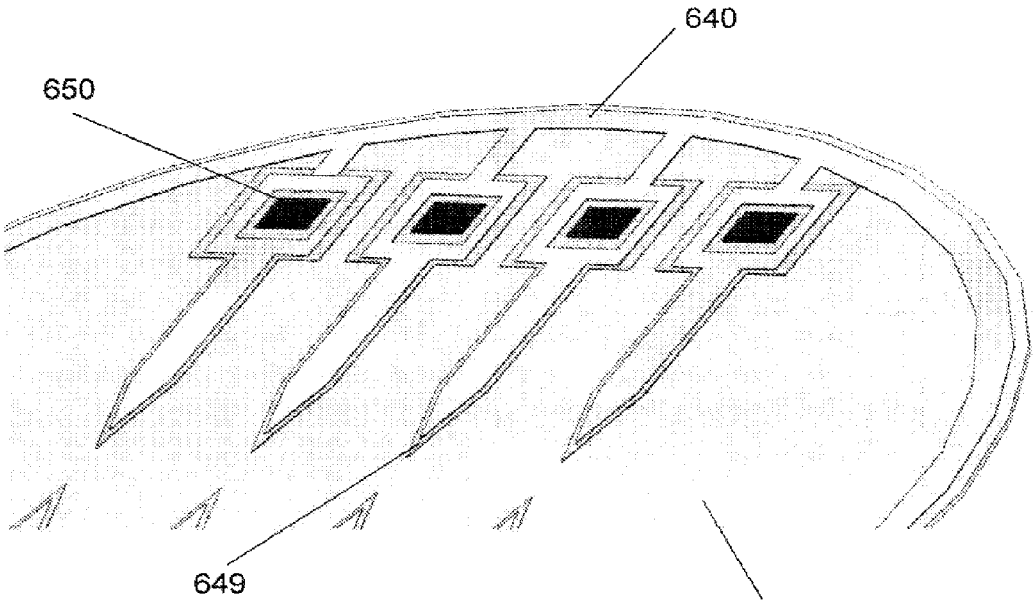
640
650
649
648

FIG. 28

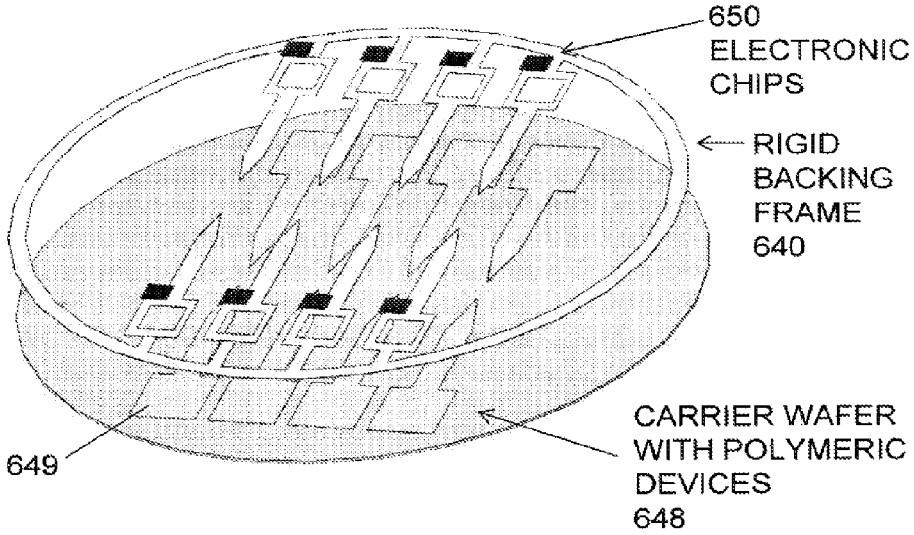
650
ELECTRONIC
CHIPS
RIGID
BACKING
FRAME
640
649
CARRIER WAFER
WITH POLYMERIC
DEVICES
648

FIG. 29

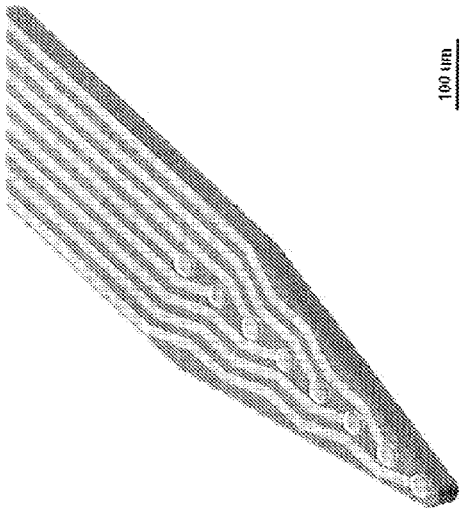

FIG. 31

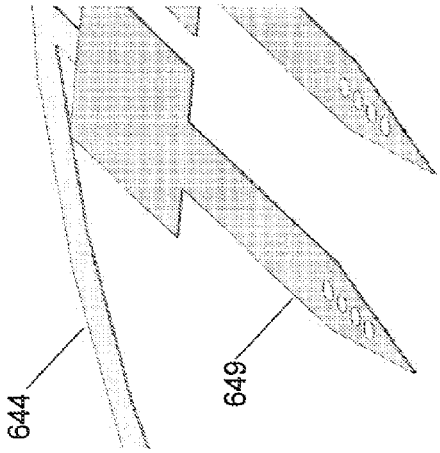

FIG. 30

FIG. 32

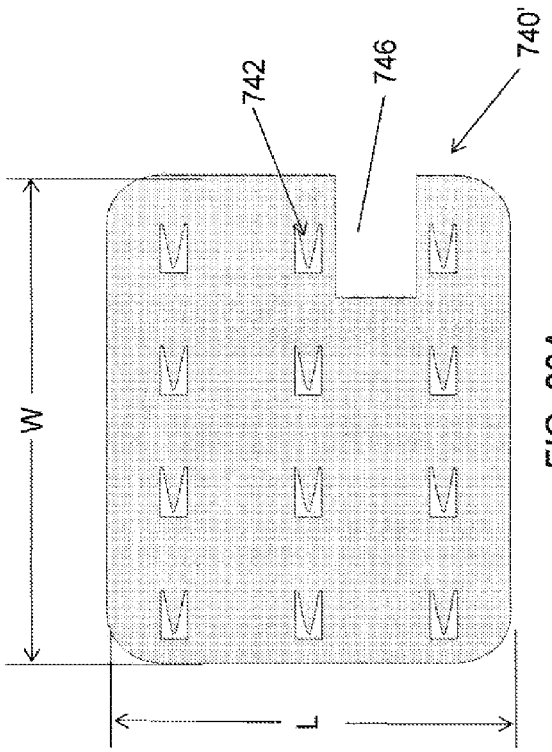

FIG. 33A

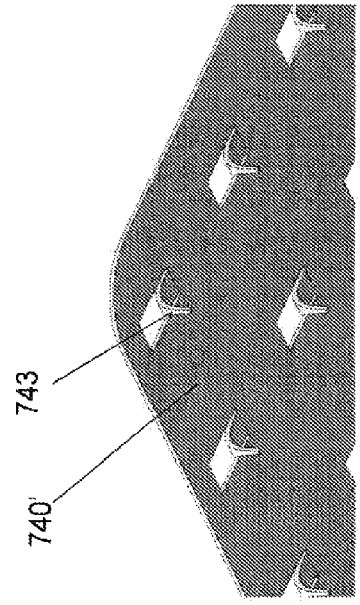

FIG. 33C

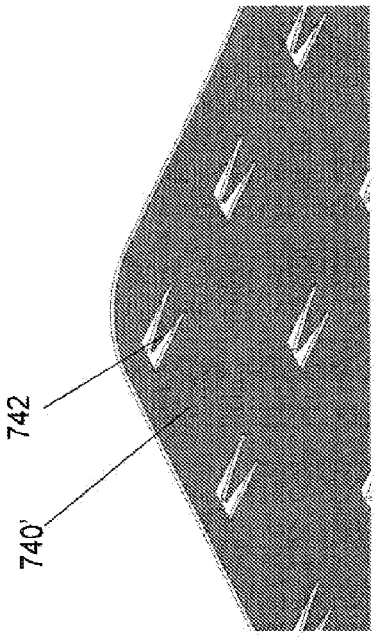

FIG. 33B

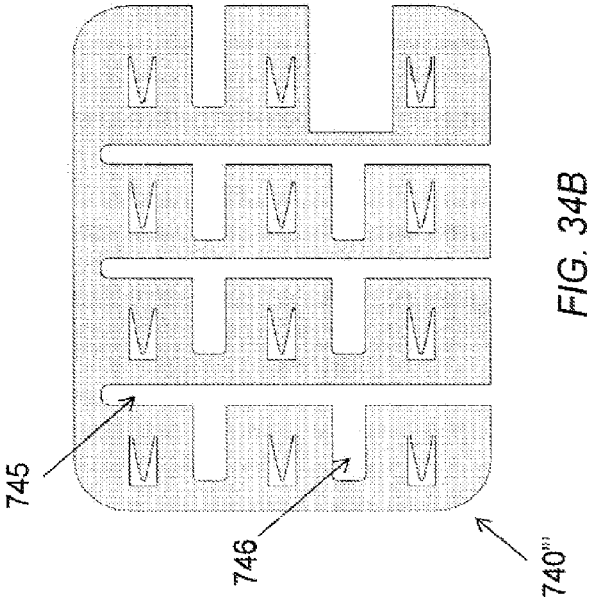

FIG. 34B

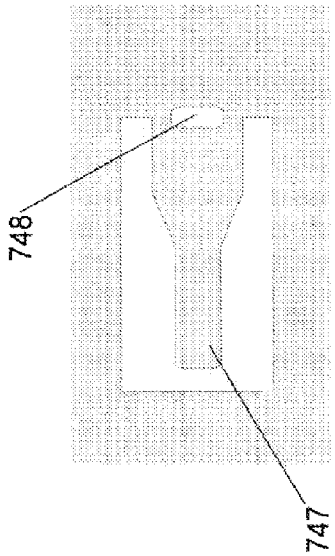

FIG. 34D

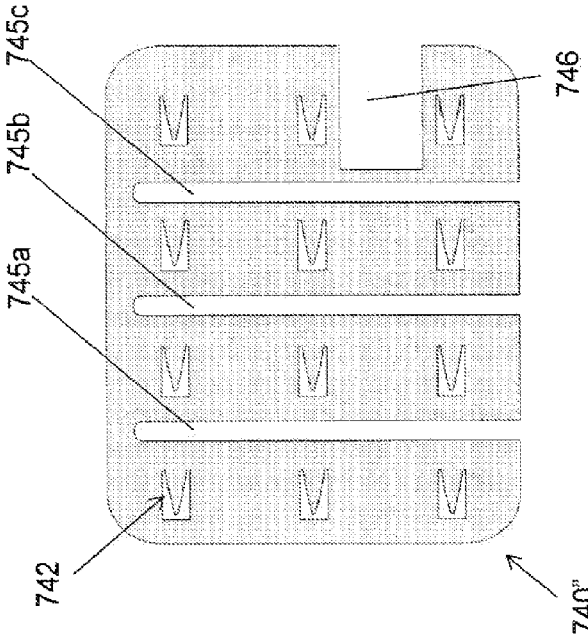

FIG. 34A

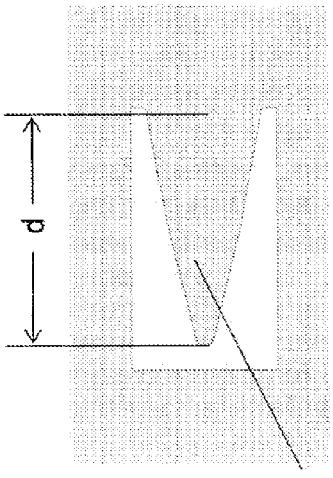

FIG. 34C

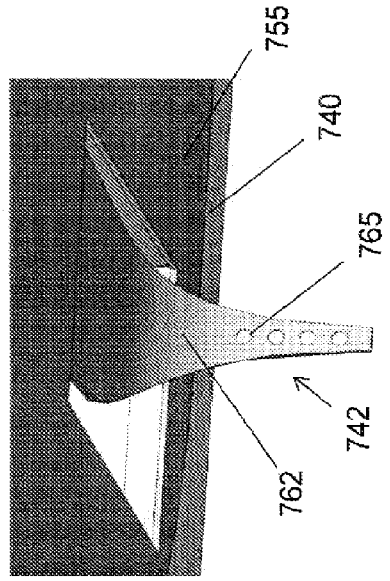

FIG. 35B

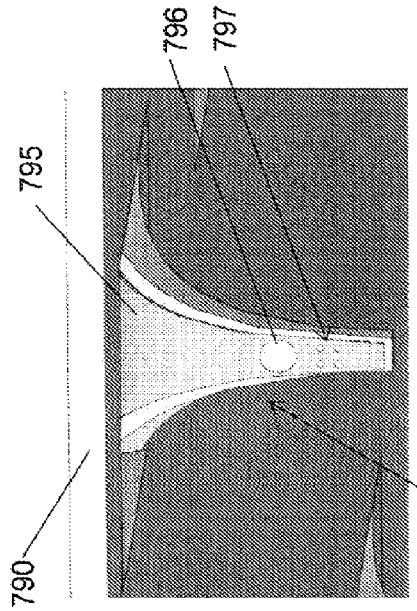

FIG. 35D

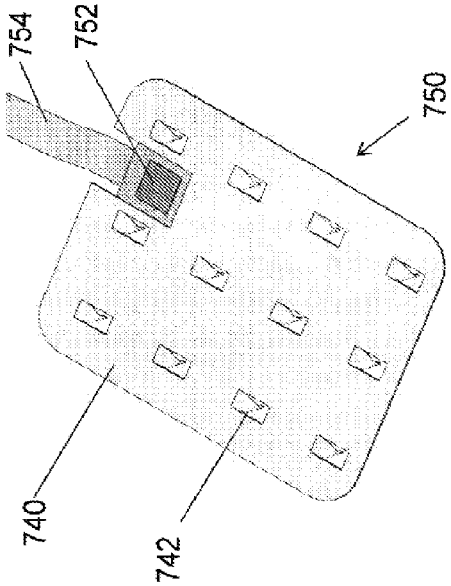

FIG. 35A

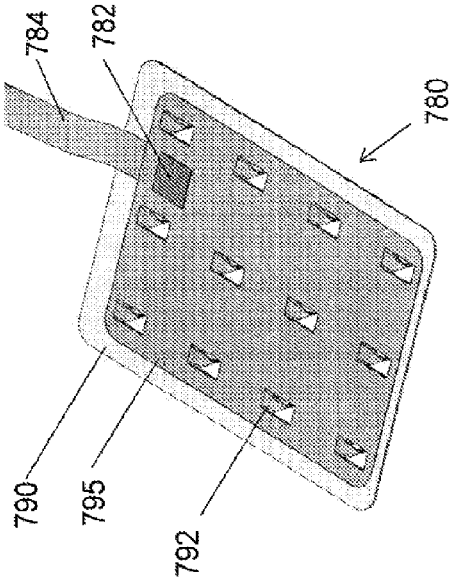

FIG. 35C

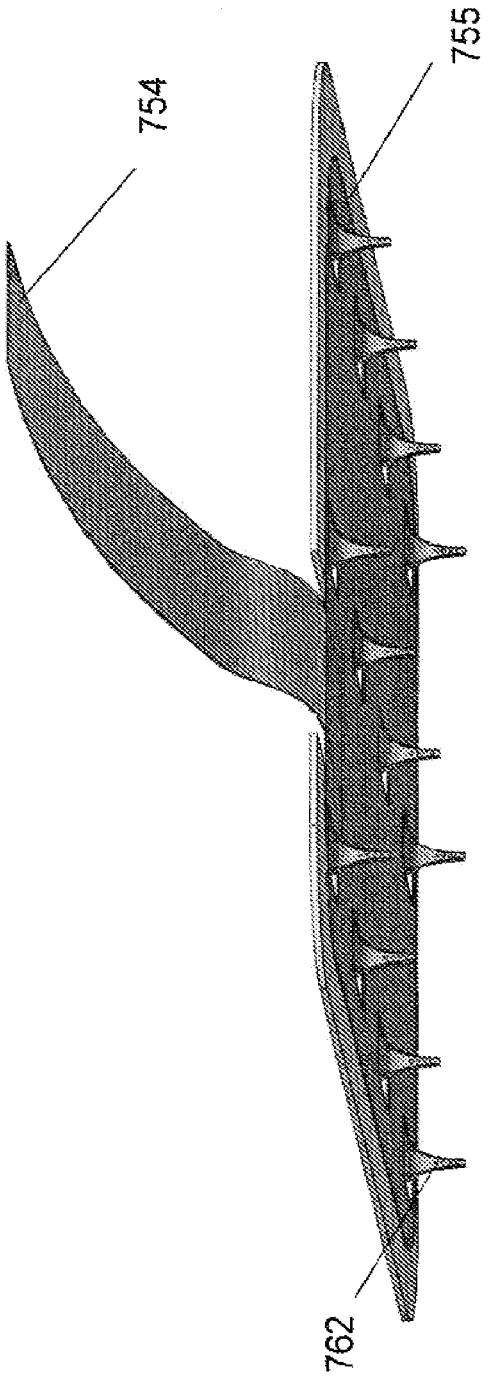

FIG. 35E

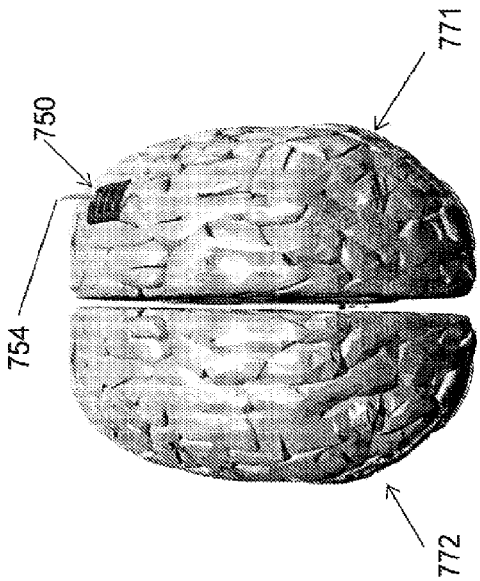

FIG. 36B

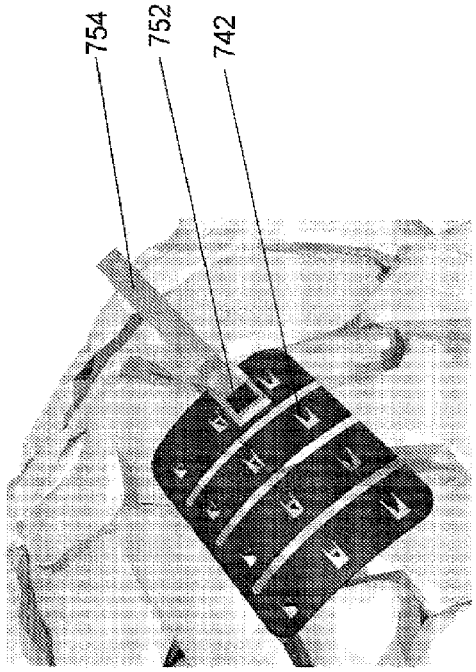

FIG. 36C

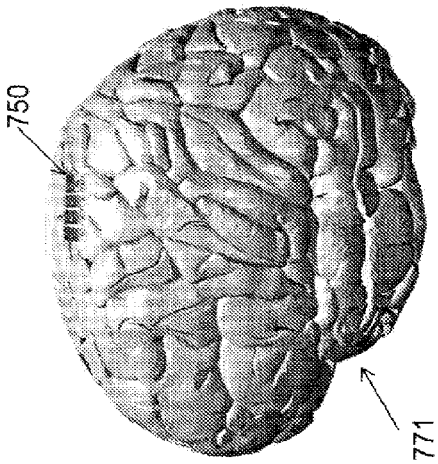

FIG. 36A

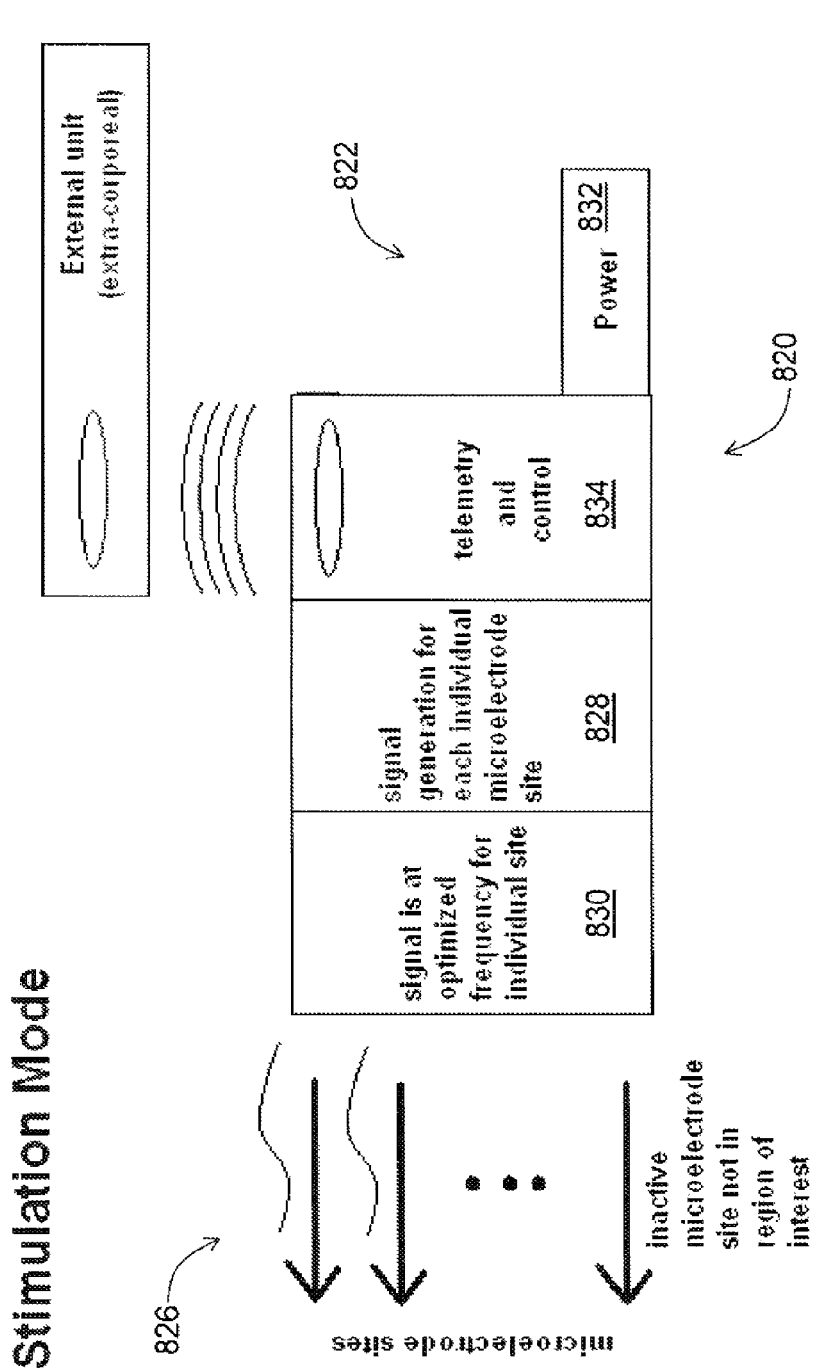
Stimulation Mode
824
External unit (extra-corporeal)
822
Power 832
820
telemetry and control 834
signal generation for each individual microelectrode site 828
signal is at optimized frequency for individual site 830
826
microelectrode sites
inactive microelectrode site not in region of interest

FIG. 37

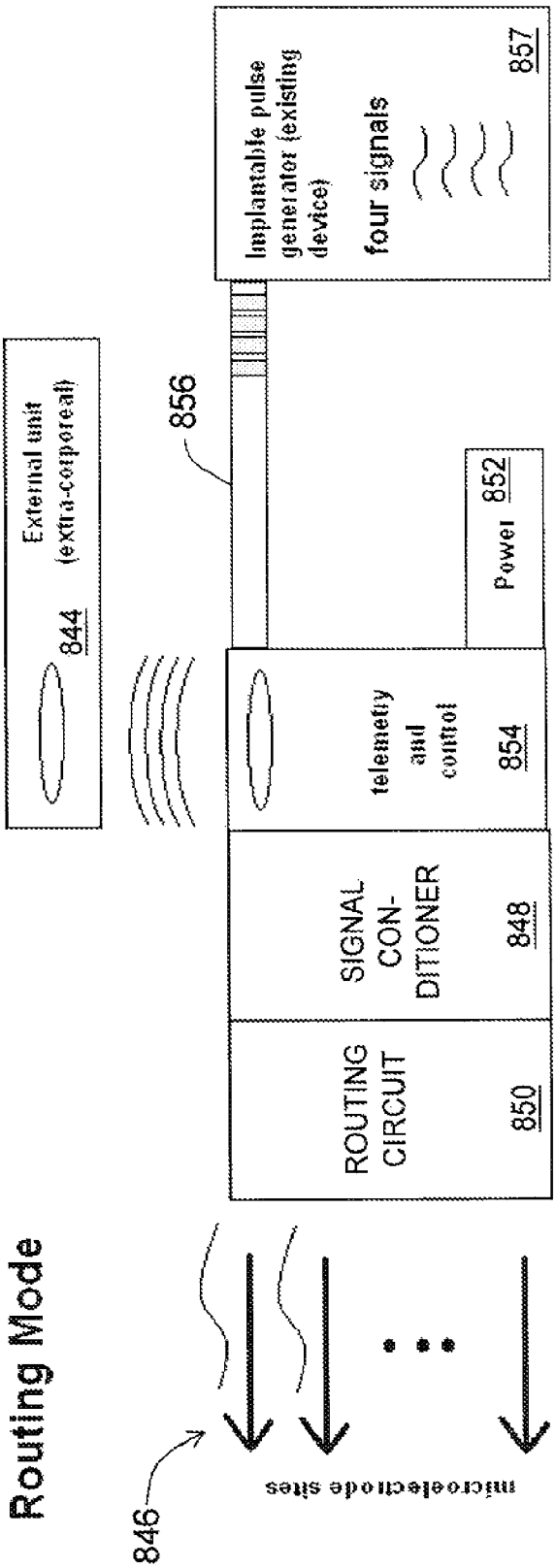
840
External unit (extra-corporeal)
844
856
Implantable pulse generator (existing device)
four signals
857
842
Power 852
telemetry and control
854
SIGNAL CON-DITIONER
848
ROUTING CIRCUIT
850
Routing Mode
microelectrode sites
846

FIG. 38

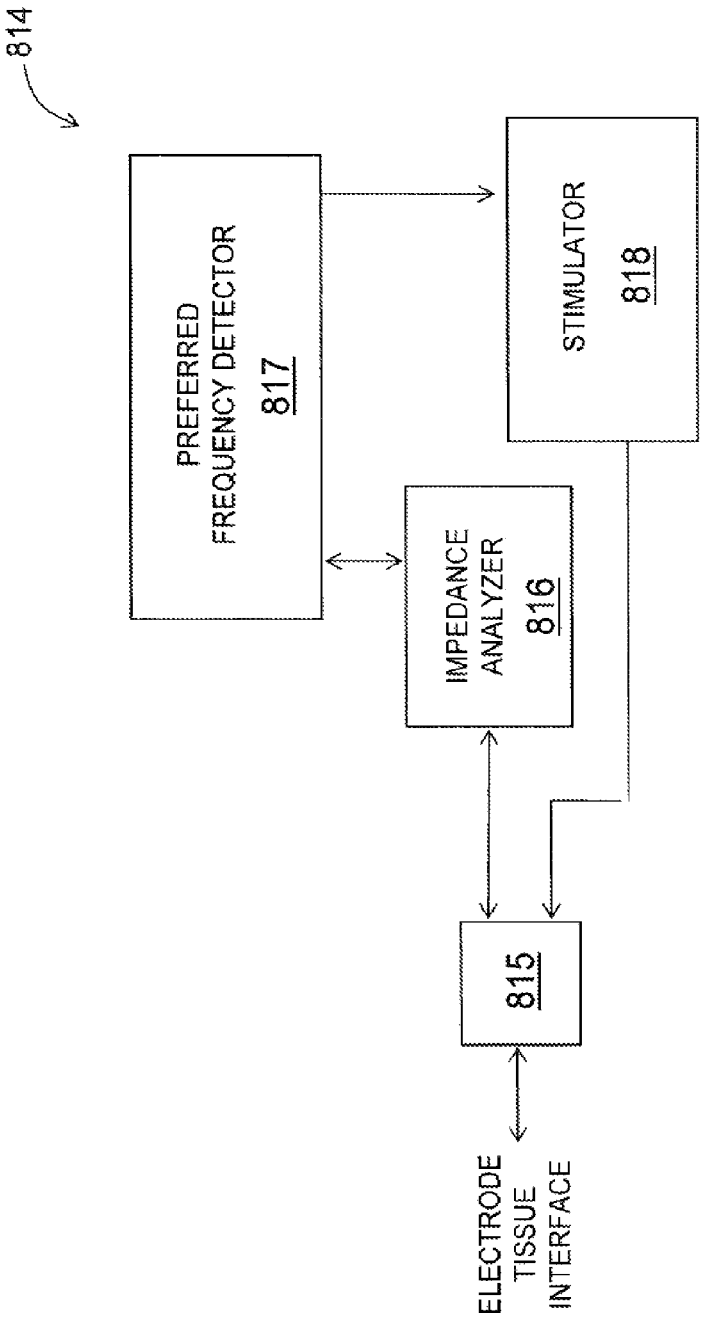
814
PREFERRED FREQUENCY DETECTOR 817
STIMULATOR 818
IMPEDANCE ANALYZER 816
815
ELECTRODE TISSUE INTERFACE

FIG. 39

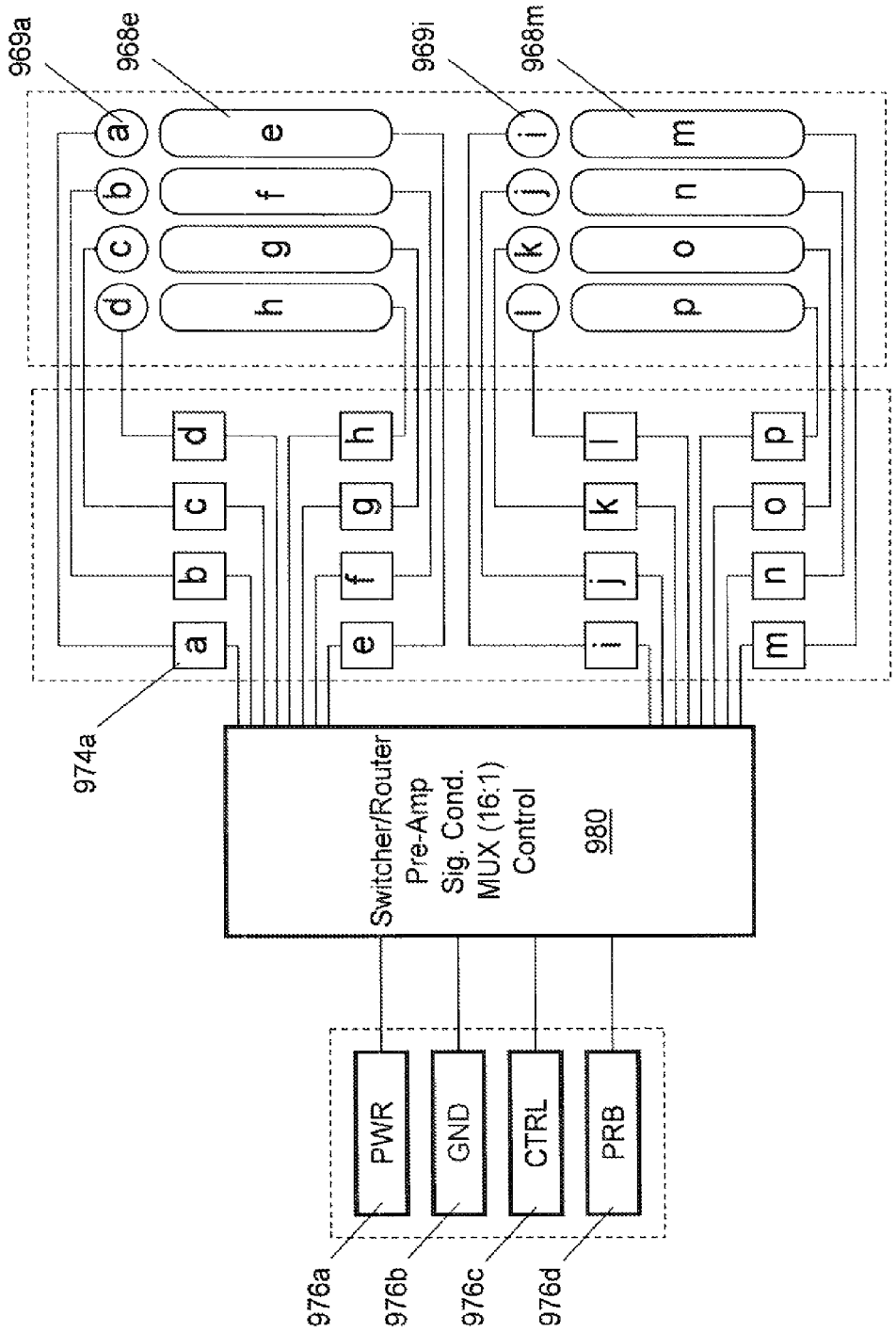
969a
968e
969i
968m
a
b
c
d
e
f
g
h
i
j
k
l
m
n
o
p
974a
Switcher/Router
Pre-Amp
Sig. Cond.
MUX (16:1)
Control
980
PWR
GND
CTRL
PRB
976a
976b
976c
976d

FIG. 40

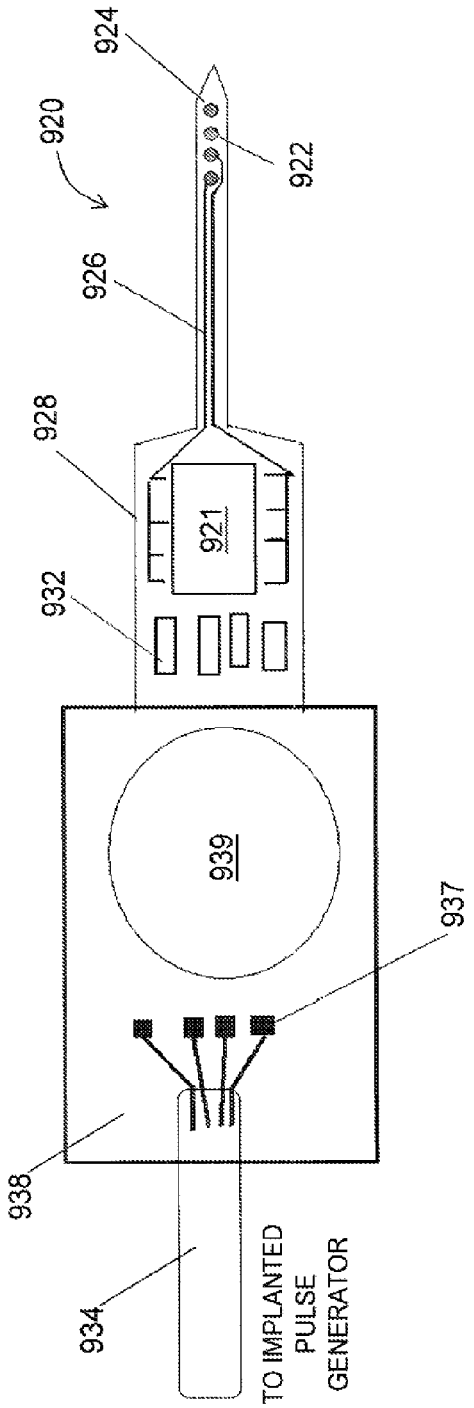

FIG. 41A

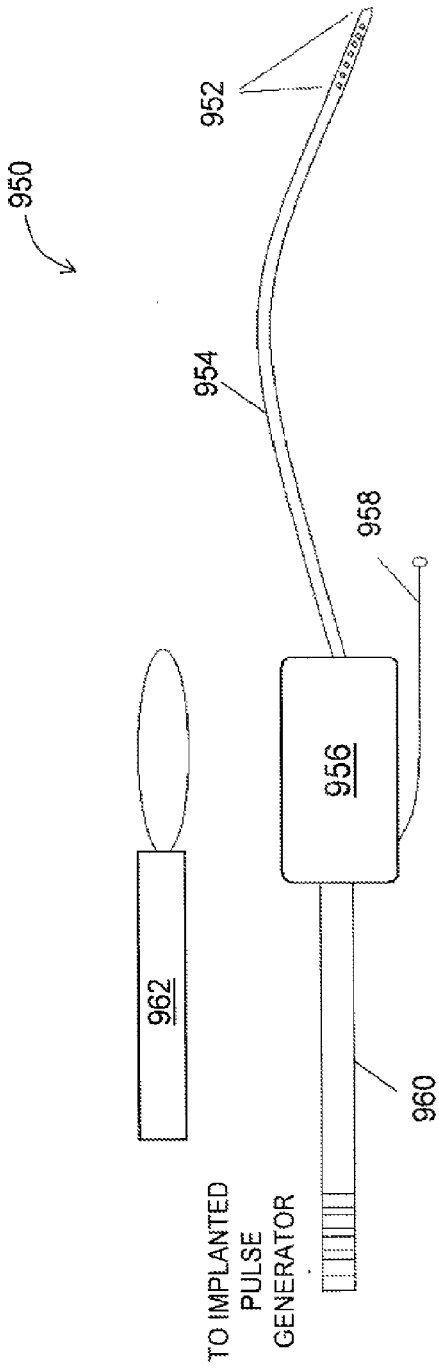

FIG. 41B

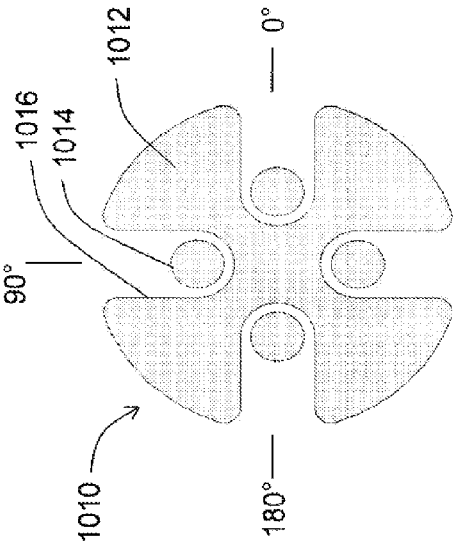

FIG. 42B

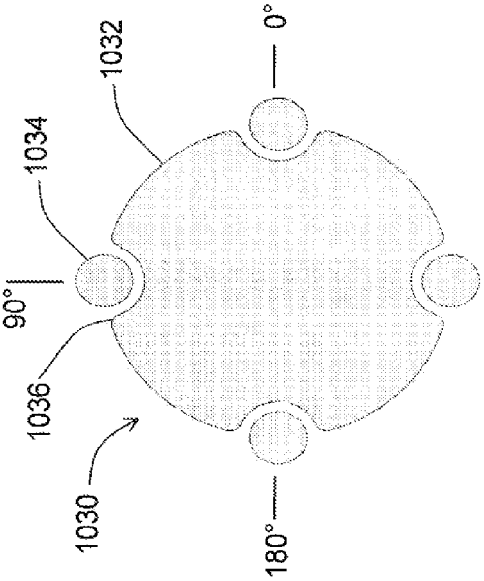

FIG. 42D

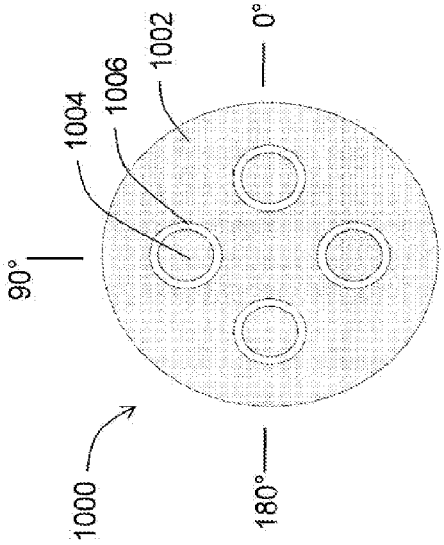

FIG. 42A

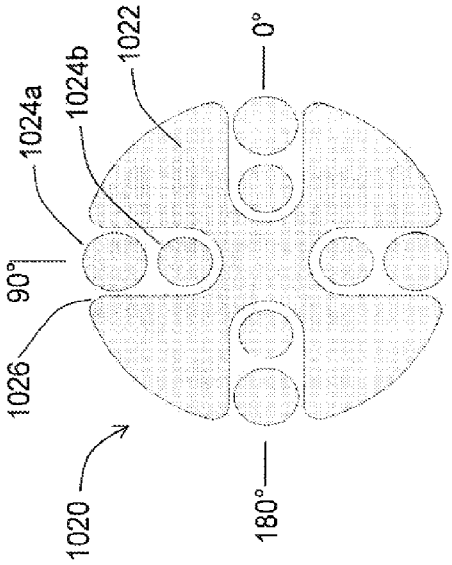

FIG. 42C

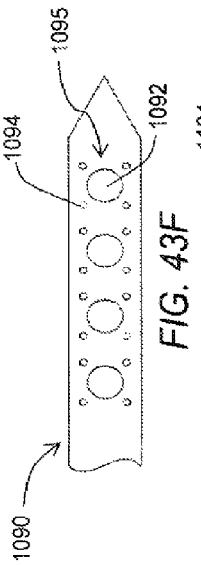

FIG. 43F

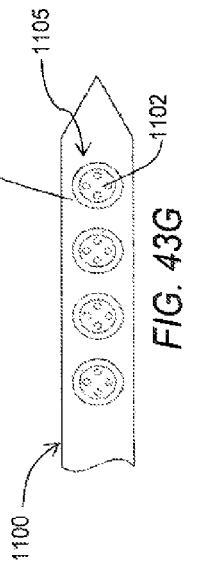

FIG. 43G

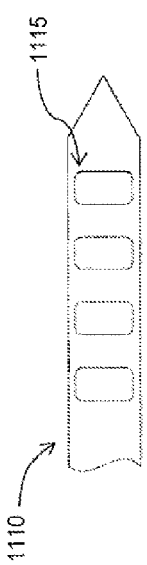

FIG. 43H

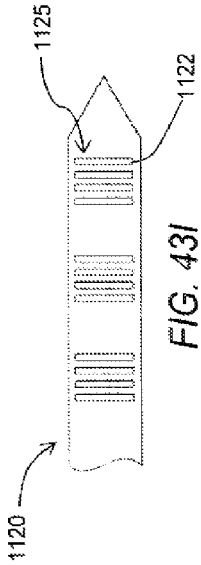

FIG. 43I

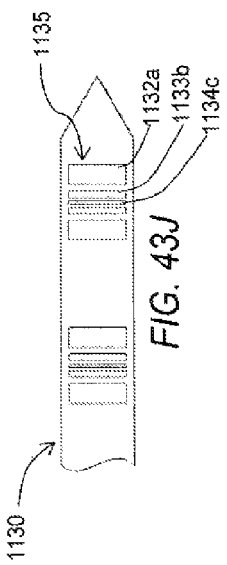

FIG. 43J

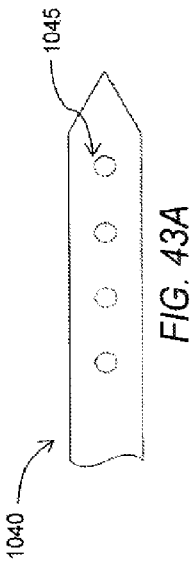

FIG. 43A

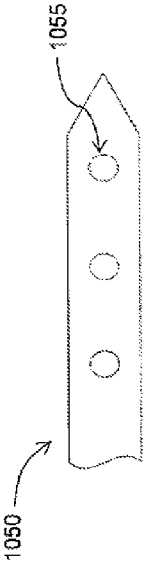

FIG. 43B

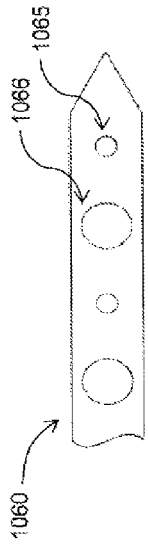

FIG. 43C

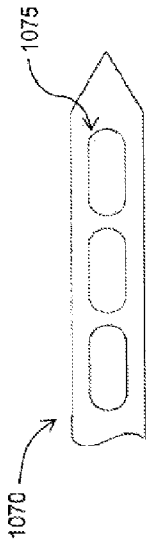

FIG. 43D

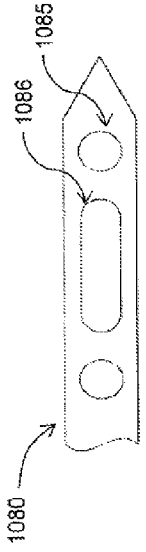

FIG. 43E

MICROFABRICATED SURFACE NEUROSTIMULATION DEVICE AND METHODS OF MAKING AND USING THE SAME

CROSS REFERENCE TO RELATED APPLICATION

The present application claims benefit of priority of U.S. patent application Ser. No. 13/512,936, which is a U.S. National Stage Application of PCT International Application Number PCT/EP2010/068658, filed on Dec. 1, 2010, which claims benefit of priority of U.S. Provisional Patent Application No. 61/265,725 filed Dec. 1, 2009. The entire contents of the foregoing applications are incorporated by reference herein.

FIELD

The present disclosure relates generally to the field of interacting with biological tissue through the use of electrical probes, and more particularly to interacting with a neurological target through the use of microelectrode probes.

BACKGROUND

Neurostimulation is a category of medical devices that are used to transfer electric charge or electrical fields to tissue and result in a physiological change which benefits the patient, or performs a physiological measurement. Neurostimulation is used today in the cochlea, the retina, the peripheral nerve system, the spine, the brain and other parts of the body.

In a particular application of Neuromodulation, conductive electrodes are placed in contact with certain cortical brain structures in order to treat certain neurological conditions. In the case of stimulating the cortical surface, for example, as described in US. Pat. App. 2008/0045775, the stimulation may relieve the symptoms of Parkinson's Disease, other movement disorders, or psychiatric disorders. In the case of stimulating an associated region of the cortical surface, for example, as described in U.S. Pat. No. 7,774,068, the stimulation can treat the symptoms of movement disorders including restless leg syndrome. In the case of stimulating the temporal love of the cortex, for example, as described in US. Pat. App. 2007/0055320 or [Theodore, W. H., Fisher, R. S., "Brain stimulation for epilepsy", *Lancet Neurology,* 3 (2), pp. 111-118, (2004).], the stimulation can treat the symptoms of temporal lobe epilepsy.

In the case where a cortical electrode array is used for recording and stimulation in long term therapy, an implantable pulse generator supplies the electrical signal to the electrode lead in contact with the brain structure. Additionally, the implantable pulse generator can record neural activity and electromagnetically transmit information outside the body. All components are placed surgically.

In the case where a cortical electrode array is used for recording and stimulation as a diagnostic tool, it may be placed temporarily on the cortex, for example for a few weeks, and then removed when no longer required. The information can be captured using wearable, or implantable, or semi-implantable, hardware.

In most prior art the electrode placed in contact with the cortex brain tissue has been metallic, disc like, and relatively large in size (e.g., 3 mm in diameter). In many cases, the electrodes are as large as the brain structures themselves. The large size of electrodes prevents specific and precise stimulation and recording of small brain targets which may be

responsible for disease. The resulting large electric fields and associated current paths stimulate other structures of the cortex, and do not concentrate on the intended target. Furthermore, these large electrodes cannot be used to identify the targets of the brain by neural-recording because the area they cover is very large.

Additionally, in most prior art, cortical electrodes are placed on the surface of dura mater which is an electrically insulating biomaterial. Placing electrodes on the dura mater, so called epidural electrode placement, prevents efficient charge transfer to and from the brain region, rendering stimulation and recording less efficacious. For example, electric fields and associated current paths established by an epidural electrode will not concentrate electrical stimulation on the intended target. This prevents the effective delivery of potentially therapeutic or diagnostic neural stimulation. Additionally, for example, neural signals that epidural electrodes are trying to capture will be very weak on the dural surface, and therefore signal-to-noise ratio will be very low. This prevents the reliable recording of diagnostically or therapeutically useful neural activity.

Current techniques that determine placement of such relatively large electrodes are accomplished by first performing a craniotomy that can vary in size but is usually at least 10 mm in diameter and be as large as several centimeters. An electrode array is then placed upon the surface of the cortex. Some surgeons may create a flap of the dura mater and place the electrode array directly on the cortical surface. Recordings of neural activity can be made using the electrode array, from several electrode contacts. This process is complex, requiring a highly skilled surgeon to place the electrode array, and usually a highly skilled neurophysiologist to interpret the neural recording data. The large craniotomies that have to be performed put the patient at risk of infection and serious collateral injury.

Attempts have been made at developing microfabricated devices specifically designed to incorporate an array of microelectrodes which can stimulate small volumes of tissue on the cortex of the brain. Attempts have also been made to develop sub-dural penetrating microelectrodes for use on the cortex of the brain, for example, as described in U.S. Pat. No. 5,215,088, "Three-Dimensional Electrode Device" by Normann et al. Additionally, descriptions have been made in [Richard et al., "A neural interface for a cortical vision prosthesis", *Vision Research,* 39, pp. 2577-2587, (1999)]. The prior devices however have not been able to easily translate to clinical use even though they have been available for more than a decade. This may be a result of the materials that are required to construct the device, because Silicon is a brittle material which may easily break during implantation or removal. Additionally, the reason for the lack of success may be because their functions do not provide enough additional information to the surgical team, because they only provide one electrode per penetrating shaft.

An important requirement for a successful outcome of cortical stimulation therapy, is the accurate placement of the stimulation and recording electrodes within the stimulation target area. Mislocation may result in unwanted side-effects, including sensory motor deficits. Additionally, a mislocated recording electrode will yield little or no relevant physiological data to the surgical team. Prior art procedures approximately localize the target by pre-surgical imaging and planning, for example through Trans-Cranial Magnetic Stimulation as described in [Komssi et al., "The effect of stimulus intensity on brain responses evoked by transcranial magnetic stimulation", *Human Brain Mapping,* 21 (3), pp. 154-164, (2004)] to identify a region of therapeutic interest.

The targets themselves may be only a few mm or less, and not be detectable through standard imaging techniques alone. Therefore exploratory surgical procedures involving acute stimulation, many times with the patient awake during the procedure, are necessary. Once the precise target area is located, the acute or chronic recording and stimulation electrodes can be implanted at the precise location.

Disadvantages of the current technology include extension of operation time by several hours, which can be an increased burden for the patient, who may be awake during such procedures, and extended cost associated with lengthier procedures which are a heavy financial burden on healthcare providers. Increased risk of surgical complications from bleeding or tissue damage caused by large craniotomies or repeatedly placed electrode arrays are a major risk of infection for the patient. Additionally, the possibility that chronic electrode arrays are not precisely located at identified target for any number of reasons, including further brain movement require that patients return to surgery.

SUMMARY

For efficient stimulation of cortical brain structures, an array of subdural penetrating microelectrodes are required. After placement of the microelectrode array, the surgeon should be able to identify the area of the brain that requires stimulation by recording from the microelectrodes. Subsequently the surgeon should stimulate the identified structure.

For more efficient diagnostic and therapeutic use in cortical brain structures, subdural penetrating microelectrodes that create a three-dimensional volume of stimulation and recording functionality are described.

The disclosure describes a system which places many microelectrode structures on the cortex of the brain, and allows the surgeon to apply a signal to each microelectrode separately, in parallel, or between at least two microelectrodes. Furthermore, using electronics to record neural activity from the system, the surgeon can develop a localized map of neural activity in the cortical region in which the electrode is implanted.

In one aspect, the disclosure relates to an implantable neurological probe. The neurological probe includes at least one protrusion on which at least one microelectrode elements are disposed on the surface of the protrusion. The microelectrode elements can perform neural stimulation or neural recording. The neurological probe preferably has several protrusions, and the protrusions preferably have several microelectrodes elements, or an array of microelectrode elements. Attached to the neurological probe, either on its surface, or connected through a tethered ensemble of wires, is the control circuitry. The control circuitry is itself encapsulated in a wearable or implantable enclosure. The neurological probe includes at least one electrical connection, or electromagnetic link, to the control circuitry. The control circuitry sends stimulation signals to the neurological probe. The control circuitry can also capture neurophysiological signals from the neurological probe. The control circuitry may connect telemetrically to yet another external controller, which can be used to transmit signals to and from the neurological probe, via the attached control circuitry.

In another aspect, the disclosure relates to a process for stimulating a neurological target. The process includes implanting a neurological probe at or near the target site on the cortex. The neurological probe itself comprises a supportive backing layer, at least one protrusion from the supportive backing layer, and at least one microelectrode element on each protrusion. Additionally, each of the at least one microelectrode elements are in electrical communication with either a proximal electrical contact, or in electrical communication with the control circuitry. The proximal electrical contact may be connected to a neurological stimulation source supplying an electrical signal. Alternatively, the control circuitry may be supplying the electrical signal to the microelectrode element. The supplied signal is applied to one or more of the microelectrode elements. The one or more energized microelectrode elements produce an electric field adapted to stimulate the neurological target site.

In yet another aspect, the disclosure relates to a process for recording from a neurological target. The process includes implanting a neurological probe at or near the target site on the cortex. The neurological probe itself comprises a supportive backing layer, at least one protrusion from the supportive backing layer, and at least one microelectrode element on each protrusion. Additionally, each of the at least one microelectrode elements are in electrical communication with either a proximal electrical contact, or in electrical communication with the control circuitry. The proximal electrical contact may be connected to a neurological recording source, such as an amplifier acquisition system. Alternatively, the control circuitry may be acquiring and recording the neurophysiological signal from the microelectrode element. The acquired signal may be transmitted from the control circuitry to the external controller. The one or more recorded microelectrode elements produce data on the electrophysiological activity of the neurological target site.

In another aspect, the disclosure relates to an implantable device comprising several neurological probes, where each neurological probes includes a supportive backing layer, at least one protrusion extending away from a surface of the supportive backing layer and at least one microelectrode element arranged along the at least one protrusion. The neurological probes may be connected to each other by tethered wires. Alternatively the neurological probes may be in telemetric communication.

In another aspect, the disclosure relates to an implantable neurological probe which includes a supportive backing layer, at least one protrusion extending away from a surface of the supportive backing layer and at least one microelectrode element arranged along the at least one protrusion.

In another aspect, the disclosure relates to a process for stimulating a neurological target by implanting a neurological probe within a vicinity of a cortical target site. The neurological probe includes a supportive backing layer, at least one protrusion extending away from a surface of the supportive backing layer. At least one microelectrode element is arranged along the at least one protrusion. The at least one microelectrode element is energized by a supplied electrical signal, wherein the at least one microelectrode element produces an electric field adapted to stimulate the neurological target site.

In another aspect, the disclosure relates to an implantable neurological surface probe includes a supportive backing layer and a number of protrusions. Each protrusion is attached at one end to the supportive backing layer and extends away from a surface of the supportive backing layer. The probe also includes a microelectrode film disposed along at least a portion of the supportive backing layer. A number of microelectrode elements are disposed on the microelectrode film and arranged along each of the number of protrusions. Each microelectrode element is disposed at a respective depth measured from the surface of the supportive backing layer.

In yet another aspect, the disclosure relates to a process of making an implantable neurological surface probe includes shaping a supportive backing layer and defining within the

supportive backing layer a number of rigid backing members. Each of the rigid backing members has a tip at one end and is attached to the supportive backing layer at another end. Each rigid backing member is bent at its attached end away from a surface of the supportive backing layer, forming a number of protrusions. A number of microelectrode elements are formed on a microelectrode film, and the microelectrode film is fastened along at least a portion of the surface the supportive backing layer. The film is fastened such that respective subsets of the plurality of microelectrode elements are arranged along each of the plurality of protrusions. When so arranged, each microelectrode element of each respective subset is disposed at a respective depth measured from the surface of the supportive backing layer.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, features and advantages of the disclosure will be apparent from the following more particular description of preferred embodiments of the disclosure, as illustrated in the accompanying drawings in which like reference characters refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the disclosure.

FIG. **1** is a perspective view of one embodiment of a cortical neuromodulation device.

FIG. **2** is a perspective view of a portion of a human anatomy illustrating an exemplary cortical neuromodulation device implanted therein.

FIG. **3** is a cross-sectional view of a portion of a human cortex anatomy illustrating an exemplary neurological surface probe positioned on the surface of the brain.

FIG. **4** is a schematic view of the components that are incorporated in the cortical neuromodulation device.

FIG. **5**A is a top view of the cortical neuromodulation device in FIG. **1**.

FIG. **5**B is detailed view of the control module of the cortical neuromodulation device in FIG. **1**.

FIG. **6**A is a detailed view of the neurological surface probe in FIG. **1**.

FIG. **6**B is an additional detailed view of the neurological surface probe in FIG. **1**.

FIG. **6**C is a perspective view of the neurological surface probe in FIG. **1** where currents have been applied to the microelectrodes.

FIG. **6**D is an additional perspective view of the neurological surface probe in FIG. **1** where currents have been applied to the microelectrodes demonstrating electric field isosurfaces.

FIG. **7**A is a front view of the neurological surface probe in FIG. **1**.

FIG. **7**B is a side view of the neurological surface probe in FIG. **1**.

FIG. **7**C is a top view of the neurological surface probe in FIG. **1**.

FIG. **8**A is a perspective view of a protrusion from the supportive backing layer of the neurological surface probe in FIG. **1**.

FIG. **8**B is an additional perspective view of a protrusion from the supportive backing layer of the neurological surface probe in FIG. **1**.

FIG. **9** is a top view of the supportive backing layer and microelectrode film that are incorporated in a neurological surface probe before they have been attached.

FIG. **10** is a top view of the supportive backing layer and microelectrode film that are incorporated in a neurological surface probe after they have been bonded.

FIG. **11**A is a perspective view of a cross section of human anatomy demonstrating the placement of the cortical neuromodulation device of FIG. **1**.

FIG. **11**B is an additional perspective view of a cross section of human anatomy demonstrating the placement of the cortical neuromodulation device of FIG. **1**.

FIG. **11**C is an additional planar view of a cross section of human anatomy demonstrating the placement of the cortical neuromodulation device of FIG. **1**.

FIG. **12** is a perspective view of an alternative embodiment of a cortical neuromodulation device.

FIG. **13** is an additional perspective view of the alternative embodiment of the cortical neuromodulation device in FIG. **12**.

FIG. **14** is a top planar view of the alternative embodiment of the cortical neuromodulation device in FIG. **12**.

FIG. **15** is a perspective view of a cross section of human anatomy demonstrating the placement of the cortical neuromodulation device of FIG. **12**.

FIG. **16** is an additional perspective view of a cross section of human anatomy demonstrating the placement of the cortical neuromodulation device of FIG. **12**.

FIG. **17**A is a perspective view of an exemplary embodiment of a circular cortical neuromodulation device.

FIG. **17**B is an additional perspective view of an exemplary embodiment of a circular cortical neuromodulation device shown in FIG. **17**A.

FIG. **17**C is a perspective view of a circular cortical neuromodulation device where currents have been applied to the microelectrodes.

FIG. **17**D is an additional perspective view of a circular cortical neuromodulation device where currents have been applied to the microelectrodes demonstrating electric field isosurfaces.

FIG. **18**A is a planar view of a component required to implement the circular cortical neuromodulation device shown in FIG. **17**A.

FIG. **18**B is a planar view of the microelectrode array film required to implement the circular cortical neuromodulation device shown in FIG. **17**A.

FIG. **18**C is a planar view of a component required to implement an alternative embodiment of the circular cortical neuromodulation device shown in FIG. **17**A.

FIG. **18**D is a planar view of the microelectrode array film required to implement an alternative embodiment of the circular cortical neuromodulation device shown in FIG. **17**A.

FIG. **18**E is a perspective view of the alternative embodiment of the circular cortical neuromodulation device components shown in FIG. **18**C and FIG. **18**D.

FIG. **19**A is a planar view of a cross section of human brain anatomy demonstrating the placement of the circular cortical neuromodulation device of FIG. **17**A.

FIG. **19**B is an additional planar view of human brain anatomy demonstrating the placement of the circular cortical neuromodulation device of FIG. **17**A.

FIG. **20**A is a planar view of human brain anatomy demonstrating the placement of a multiplicity of circular cortical neuromodulation devices of FIG. **17**A.

FIG. **20**B is a detailed perspective view of human brain anatomy demonstrating the placement of a multiplicity of circular cortical neuromodulation devices of FIG. **17**A.

FIG. **21**A is a perspective view of an additional embodiment of a circular cortical neuromodulation device.

FIG. **21**B is an additional perspective view of the circular cortical neuromodulation device shown in FIG. **21**A.

FIG. **21**C is planar view of the circular cortical neuromodulation device shown in FIG. **21**A.

FIG. **22** is a perspective view of human brain anatomy demonstrating the placement of a circular cortical neuromodulation device of FIG. **21**A.

FIG. **23** is a detailed perspective view of human brain anatomy demonstrating the placement of a cortical neuromodulation device of FIG. **21**A.

FIG. **24** is a detailed perspective view of human brain anatomy demonstrating a multiplicity of implanted circular cortical neuromodulation devices of FIG. **21**A

FIG. **25**A through FIG. **25**M illustrate cross sections of an exemplary microelectrode device at various different stages of construction according to an exemplary fabrication procedure.

FIG. **26** is a micrograph of an embodiment of a microelectrode.

FIG. **27** is a planar view of a construction element of an embodiment of a microelectrode tip.

FIG. **28** is a schematic view of a portion of the construction element illustrated in FIG. **27**.

FIG. **29** is an exploded schematic view of a construction element of an embodiment of a microelectrode tip.

FIG. **30** is a schematic view of another portion of the construction element.

FIG. **31** is a perspective view of a distal portion of a microelectrode tip.

FIG. **32** is a cross sectional view of the distal portion of the microelectrode tip illustrated in FIG. **31**.

FIG. **33**A is a planar view of a construction element of a microelectrode array assembly.

FIG. **33**B is a perspective view of a construction element of a microelectrode array assembly.

FIG. **33**C is a perspective view of a construction element of a microelectrode array assembly shown in FIG. **33**B after the rigid backing members have been assembled into position

FIG. **34**A is a planar view of a construction element of a microelectrode array assembly.

FIG. **34**B is a planar view of a construction element of a microelectrode array assembly.

FIG. **34**C is a more detailed planar view of a construction element of a microelectrode array assembly.

FIG. **34**D is a more detailed planar view of an alternative embodiment of a construction element of a microelectrode array assembly.

FIG. **35**A is a perspective view of a microelectrode array assembly.

FIG. **35**B is a more detailed perspective view of a microelectrode array tip.

FIG. **35**C is a perspective view of an alternative embodiment of microelectrode array assembly.

FIG. **35**D is a more detailed perspective view of an alternative embodiment of a microelectrode array tip.

FIG. **35**E is a perspective view of the microelectrode array assembly shown in FIG. **35**A.

FIG. **36**A is a view of a portion of a human anatomy illustrating an exemplary microelectrode structure positioned at a neurological target.

FIG. **36**B is an additional view of a portion of a human anatomy illustrating an exemplary microelectrode structure positioned at a neurological target.

FIG. **36**C is a more detailed view of a portion of a human anatomy illustrating an exemplary microelectrode structure positioned at a neurological target.

FIG. **37** is a functional block diagram of an exemplary embodiment of a neurological microelectrode system configured in stimulation mode.

FIG. **38** is a functional block diagram of an exemplary embodiment of a neurological microelectrode system configured in routing mode.

FIG. **39** is a functional block diagram of another embodiment of a neurological microelectrode system.

FIG. **40** is an electronic circuit schematic diagram for an exemplary on board microelectronic circuit.

FIG. **41**A is a schematic view of an embodiment of a neurological target stimulator.

FIG. **41**B is a schematic view of an embodiment of a neurological target stimulator system.

FIG. **42**A through FIG. **42**D are a schematic views of various alternative embodiments of a microelectrode array.

FIG. **43**A through FIG. **43**J are schematic views of various alternative embodiments of a cortical depth microelectrode array.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Described herein are microelectrode array devices, and methods of fabrication and use of the same, to provide highly localized and efficient electrical stimulation of a neurological target, such as individual neurons, groups of neurons, and neural tissue as may be located in an animal nervous system, such as the human cortex. In indications where it is difficult to determine the final positioning of the microelectrode for diagnostic or therapeutic use, it is beneficial to safely implant many electrodes in the target region, and then proceed to determine the best electrode by applying an electrical signal for neural stimulation or performing neural recording. A higher number of microelectrodes, and more specifically a higher number of microelectrode in a three-dimensional volume, will increase the probability that the best therapeutic or diagnostic region is in contact with a microelectrode.

The stimulation can be highly localized, because the microelectrode elements can be as small as only 2 μm or large as 2 mm in either of diameter or width. The relative spacing between such microelectrode elements can also be as small as only 2 μm or as large as 2 mm. Although 2 μm are indicated as lower limits to either dimension or spacing, other embodiments are possible having dimensions and/or inter-element spacing of less than 2 μm, as may be practically limited by fabrication techniques. Generally, microelectrodes in the form of a disc of about 100 μm in diameter, with about a 500 μm spacing are particularly efficient in recording from neural tissue in the cortex. Additionally, microelectrodes in the form of a disc of about 300 μm diameter, with about a 500 μm spacing are particularly efficient in stimulating neural tissue in the cortex. An array of such microelectrode elements may consist of one or more such elements (e.g., four elements), each disposed at a respective position along a support structure. There is additionally an array of support structures that can be all be arranged to protrude from a supportive backing. In this manner, a multiplicity of microelectrode elements can be arranged in three-dimensional space. This is in contrast to currently available epidural recording and stimulation leads, such as the RNS® System from NeuroPace Corp. (Mountain View, Calif.) which may be marketed in the future. Additionally, grid and strip electrodes are marketed for transient use from Integra Corp. (New Jersey, N.J.). Such commercially available devices include relatively large, disc electrodes measuring about 3 mm in diameter, with large spacing between each electrode (i.e., 5 mm) and only generate a two

dimensional area of targeting in the epidural region of the cortex. It would be beneficial to have a system that can provide a three-dimensional volume of influence in the subdural area of the cortex, in order to perform better neural recording and provide more efficacious neural stimulation.

Smaller microelectrode elements can be used to provide neurological stimulation that is highly localized and efficient because an array of such microelectrodes can also be used to identify the stimulation region of interest. For example, one or more microelectrode elements of such an array of microelectrode elements can be used to detect and, in some instances, record neuronal activity in the vicinity of the detecting/recording microelectrode elements. Such refinement offered by the relatively small size and/or spacing of the microelectrode elements can be used to obtain a highly localized map of neuronal activity in the three-dimensional volume surrounding the implant. A suitably dimensioned microelectrode array, and a suitably dimensioned supportive backing layer, can have multiple microelectrode elements positioned in a general vicinity of a neurological target. The array can therefore be used to locate a precise neurological target without further repositioning, by identifying those one or more microelectrode elements located in a very specific region of the neurological target. The microelectrode array can be programmed to stimulate in a very specific region, for example, using only a certain number of the microelectrode elements to actively stimulate the surrounding neurons and/or neuronal tissue, while other electrode elements of the array remain inactive.

In some embodiments, a three-dimensionally arranged neurological surface probe includes such a multiplicity of microelectrode arrays having elements with relatively small size and/or spacing that can be used to obtain a highly localized map of neuronal activity in the region surrounding the implant. For example, such a device configured with a several linear arrays of microelectrodes can be surgically placed onto the surface of the patient's brain (i.e., the cortex). Preferably, the elements of the microelectrode arrays span a region including the neurological target. Neurological activity can then be independently detected by one or more of the microelectrode elements. The detected activity may be captured in a recorder or display device, allowing a clinician to identify which one or more of the microelectrode elements is positioned closest to the intended target. Beneficially, location of the target can be determined without any repositioning of the elongated device, thereby simplifying the medical procedure and reducing patient risk.

In some embodiments, the device is used only transiently, or acutely, being removed after the target has been located, being replaced with a chronic probe, positioned at the determined target location. Alternatively or in addition, the device itself can be left in place as a chronic device, the same microelectrodes, or different ones, being used to record and/or stimulate the neurological target over an extended period.

One embodiment of a neurological surface probe illustrated in FIG. **1** includes a neurological device assembly referred to as a cortical neuromodulation device **100**. The cortical neuromodulation device **100** includes a neurological surface probe **101** and a control module **150**. The neurological surface probe **101** is located on the distal portion of the cortical neuromodulation device **100**, and the control module **150** is located on the proximal portion of the cortical neuromodulation device **100**. The neurological surface probe **101** is comprised of two components, the supportive backing layer **120** and the microelectrode array film **110**. In this embodiment nine protrusions from the neurological surface probe are referred to as cortical depth probes **130**. On the surface of each cortical depth probe is a linear array of microelectrode elements **140**. The neurological surface probe **101** is attached to the control circuitry **150** via a ribbon cable tether **180**. The control module **150** is comprised of a lower housing **151** and an upper housing **152**. The lower housing **151** may also incorporate at least one fixation structure **156** which is used to fix the control module **150** the skull. In the current embodiment three fixation structures **156***a*, **156***b*, **156***c* are provided which incorporate through holes for cranial fixation screws. Inside the control module **150** is the control circuitry **160** which is comprised of an electronic circuit. In the current embodiment the control circuitry **160** is comprised of three individual and interconnected control circuits **160***a*, **160***b*, **160***c*. Additionally, inside the control module **150** a loop antenna **165** is connected to the control circuitry **160** and is used to communicated information to and from the control module **150** extracorporeally. In the exemplary embodiment, each of the microelectrode elements **140** is in electrical communication with the control circuitry **160** via a respective electrical conductor disposed in the microelectrode array film **110** and the ribbon cable tether **180**. In use, stimulation signals are directed from the control circuitry **160** to the microelectrode elements **140**. Additionally, in use, recorded neurophysiological signals are directed from the microelectrode elements **140** to the control circuitry **160**. Furthermore, in use, the control circuitry **160** is programmed to function by an external control system (not shown) through the loop antenna **165**. The control circuitry **160** can also transmit information about the recorded neurophysiological signals to the external control system (not shown) through the loop antenna **165**.

The size and shape of the control module **150** can vary, but is generally intended to be implanted on the surface of the skull. The size and shape of the neurological surface probe **101** can vary, but is generally intended to be implanted on the surface of the cortex. The size and shape of the cortical depth probes **130** can vary, but are generally intended to penetrate the layers of the cortex. Finally, the size, shape, and quantity of the microelectrode elements **140** can vary, but are generally intended to record from the cortical layers and stimulate the cortical layers. The neurological surface probe **101** is shown as a square. Alternatively, in some embodiments the neurological surface probe **101** is circular. Alternatively, in some embodiments the neurological surface probe **101** is rectangular. The neurological surface probe **101** is shown with all cortical depth probes **130** descended and protruding from its surface. Alternatively, in some embodiments not all of the cortical depth probes **130** are descended. Alternatively, in some embodiments the cortical depth probes **130** are descended only at the time of surgery, once the surgeon has decided which cortical depth probes **130** are necessary.

The cortical neuromodulation device **100** is preferably sized and shaped for its intended neurological application. The cortical neuromodulation device **100** is not limited for use in the animal or human cortex. For example, the cortical neuromodulation device **100** may be at least partially placed within the central nervous system. Alternatively or in addition, the cortical neuromodulation device **100** may be used within other parts of the body, such as the retina, the cochlea, the epidural space of the spine, the spine, and other locations within the peripheral nervous system. Thus the diameter and length of the cortical neuromodulation device **100** may vary depending on the particular anatomical target. Additionally, the configuration of the neurological surface probe **101** and the cortical depth probes **130** are sized and shaped for an intended neurological target. The number, shape, orientation, size, and spacing of the microelectrode elements **140** can be defined in response to the intended neurological target.

In at least some embodiments one or more of the microelectrode elements **140** are sized and or spaced to record from and/or stimulate a single neuron, or group of neurons. The cortical neuromodulation device **100** can be used to detect and/or record neuronal activity at the neurological target. Neuronal activity naturally occurring within the neurological target gives rise to local electromagnetic fields that can be detected by one or more of the microelectrode elements **140** of the cortical depth probe **130**. For example, electric fields produced by neurons will polarize one or more of the microelectrode elements **140**. Such polarization gives rise to an electrical potential with respect to a reference, such as electrical ground, or another one of the microelectrode elements **140**. Such electric activity can be further conducted to the control circuitry **160** through the internal electrical conductors in the ribbon cable tether **180**. The control circuitry **160** can then electromagnetically transmit captured data of the detected electrical activity for further processing by an external controller (not shown). For example, the captured data can be displayed on a computer.

Alternatively or in addition, one or more of the microelectrode elements **140** can be used to electrically stimulate the neurological target. For example, one or more electrical signals generated by the control circuit **160** can be applied to one or more of the microelectrode elements **140**. These electrical signals can be conducted through the internal electrical conductors in the ribbon cable tether **180** to one or more of the microelectrode elements **140** of the microelectrode array film **110**. Depending on the amplitude and polarity of the electrical signals, an electrical field will be induced by the polarized microelectrode elements **140**. Electrical fields induced by such polarization can interact with one or more neurons at the neurological target.

In some embodiments, at least a portion of the control module **150** can be extracorporeal. Alternatively or in addition, the stimulation source can be implanted in the body. Any implanted elements of the stimulation source are preferably fabricated and/or contained with a hermetically sealed, biocompatible envelope. Such bio-compatible packaging of signal sources is well known, for example, in the area of artificial pacemakers. The stimulation source, when provided, may be a controllable signal generator producing a desired signal according to a prescribed input. For example, the signal generator may receive an input indicative of a desired output stimulation signal frequency. Such output stimulation signals can have a variety of wave forms, such as pulses, charged balanced pulses, sinusoidal, square wave, triangle wave, and combinations of such basic wave forms.

In some embodiments, the stimulation source includes a pulse generator for applying signals to the microelectrode elements **140**. The signals from the pulse generator can be connected directly to the microelectrodes, or they can be preprocessed using electronics. In some embodiments, such preprocessing electronics are embedded within the implantable device. The preprocessing electronics can filter certain parts of an original signal, such as a cardiac pacemaker signal, in order to select preferred frequency components of the original signal that are at or near a peak resistance frequency of the microelectrodes. For embodiments in which there are more microelectrodes than signals, electronics can route the stimulation signals to preferred one or more of the microelectrodes.

Microfabricated Components

A microfabrication procedure can be used to implement electrically conductive traces within an insulative substrate to form any of the microelectrode array devices described herein, whether the array devices are rigid or flexible. The microfabricated components include portions of the microelectrode array assembly. The microelectrode array can be implemented in a polymeric material such as polyimide or parylene and includes thin film or plated layers of a metal or metal oxide with high charge transfer capability such as platinum, platinum-iridium, iridium, iridium oxide or titanium. In some embodiments, other metals, metal alloys, carbon based conductive materials, and electrically conductive materials, such as doped semiconductors, conductive polymers, and conductive ceramics may be used. In some embodiments, the polymeric and metallic layers are deposited sequentially and formed using established principles of microfabrication such as spin coating, DC/RF sputtering, photolithography, plasma etching, and etching with a mask consisting of a secondary or sacrificial material such as silicon dioxide or photosensitive resist.

The metallic layer is formed to create one or more of the microelectrode array elements and electrically conductive traces that connect the array elements to one or more of the electronics. In some embodiments, the microelectrode array includes multiple layers. For example, the polymeric layers serve to isolate the traces from each other, while also providing the structure of the implant's stimulating/recording tip. There are several fabrication methods which can be described to build such a microfabricated component.

The insulative substrate can be a polymer, such as a polyimide or parylene but can also be polyurethane or polysiloxane (silicone), or any other suitable insulator. For substantially non-flexible, or rigid embodiments, a rigid or semi-rigid substrate can be included. In some embodiments, the microelectrode array film **110** is formed on at least one surface of a rigid substrate, such as a planar ceramic member. Alternatively or in addition, one or more rigid or semi-rigid supporting members can be attached during fabrication to provide a desired amount of rigidity. Generally, the microfabricated component can be fabricated, for example, using a series of additive and subtractive processes that produce a stack of materials.

The supportive backing layer **120** provide a rigid or semi-rigid support to the microelectrode array film **110**. It can be implemented in a variety of biocompatible materials, such as stainless steel, polyimide, or polyetheretherketone (PEEK). The supportive backing layer can be structured using laser micromachining processes, stamping, forming, or injection molding methods. In the case that the supportive backing layer **120** is of a conductive material, it may also form electrical ground for the stimulation or recording of signals. The supportive backing layer **120** is generally a relatively thin structure, between 50 um to 2 mm. The supportive backing layer **120** should be amenable to being slightly deformed in order to create protrusions from its surface, such as the case with the cortical depth probes **130** that it supports.

Mechanical components of the cortical neuromodulation device **100** include the supportive backing layer **120**, and the control module **150**. In some embodiments, the control module **150** may be implemented directly on the surface of the neurological surface probe **101**. In the current embodiment it is implemented separately, but is attached via a ribbon cable tether **180**. Alternatively, in some embodiments there is no control module **150**, and the electrical conductors embedded in the microelectrode array film **110** and the ribbon cable tether **180** are connected directly to an external system through the patient's skin.

The electrical components can be discrete or microelectronic parts. Their purpose is to filter, route, generate, or process signals to and from the microelectrode elements **140**. They can be attached to the control circuit **160** during pro-

duction, or bonded afterwards. Alternatively, the can be bonded directly to the microelectrode array film **140**. The loop antenna **165** is intended to transmit and receive signals in the control circuitry. All electrical components are generally contained within the control module **150**.

The cortical neuromodulation device **100** can be implanted near a neurological target, such as a target brain structure, using common neurosurgical techniques such as stereotaxy or endoscopy. The cortical neuromodulation device **100** can be inserted without support, or attached to a stereotactic tool. Generally, the neurological surface probe **101** will be implanted in one surgical step, while the control module **150** will be implanted in an additional surgical step. The neurological surface probe **101** is intended to be implanted subdurally, through a craniotomy. The cortical depth probes **130** are intended to be rigid enough to penetrate the dura mater. However, the surgeon may also decide to create a flap of the dura mater during surgery, and thereby the neurological surface probe **101** will be implanted subdurally. The control module **150** is intended to be implanted on the surface of the skull and fixated to the bone matter using screws.

A clinician can direct the captured neurological recordings from the microelectrode elements **140** to a display unit. The information can be transmitted wirelessly using the loop antenna **165**. Alternatively, in the case that the cortical neuromodulation device **100** does not include a control module **150**, the information can be transmitted directly through the ribbon cable tether **180** to an external controller (not shown). The recorded data allows a clinician to identify certain regions of the brain according to their electrical activity. In some embodiments, such recording information can be processed automatically. The processing, or part of the processing, can be performed by the control circuit **160** before transmitting it wirelessly to an external controller. Alternatively, in the case that the cortical neuromodulation device **100** does not include a control module **150**, the processing is performed entirely by the external controller (not shown). The microelectrode elements **140** used to record from the brain can be the same microelectrode elements **140** as those used to stimulate tissue. The recording electrodes can also be separate from those used to stimulate the brain. This situation might be preferred because electrodes destined for recording may be different in size and design than those for stimulation.

A perspective view of the portion of a human anatomy is illustrated in FIG. **2**, showing implantation of an exemplary cortical neuromodulation device **100** positioned for interaction with a neurological target **200** located on the cortex of the human brain **220**. The distal portion of the cortical neuromodulation device **100** is the neurological surface probe **101** and is positioned at the neurological target **200**, in this instance located within the human brain **220**. In this embodiment the proximal end of the cortical neuromodulation device **100**, i.e., the control module **150**, is attached to the distal end through a ribbon cable or wire bundle. This minimizes the size of the device implanted directly in the brain. In some embodiments the control module **150** is small enough to be integrated directly with the neurological surface probe **101**. Alternatively, the control module **150** can be implanted at a remote portion of the subject body **210**, such as the upper chest. One or more cortical neuromodulation devices **100** can be implanted in different cortical brain regions.

Referring now to FIG. **3**, a cross-sectional view of a portion of a human brain anatomy **200** is shown, illustrating an exemplary neurological surface probe **101** positioned at a neurological target **200** (e.g., the cortex as shown). The neurological surface probe **101** includes an array of nine cortical depth probes **130**. On the surface of each cortical depth probe **130** is an array of microelectrode elements **140** distributed linearly. In this exemplary embodiment, there are four microelectrode elements **140** on each cortical depth probe **130**. Preferably, the cortical depth probe **130** and microelectrode elements **140** are shaped and sized to allow one or more of the microelectrode elements **140** to be positioned in a clinically relevant cortical layer **201***a* **201***b* or **201***c* (collectively **201**). Additionally, in some embodiments, it may be advantageous for the device to fit between two sulci **205**, the natural folds of the cortex. This is important in terms of safety for the patient.

As illustrated, one or more of the microelectrode elements **140** (on the cortical depth electrodes **130** protruding from the neurological surface probe **101**) are positioned in direct contact with the neurological target **200**. The planar component of the neurological surface probe **101** remains on the surface of the brain **221**. In some surgical procedures the planar component of the neurological surface probe **101** remains above the dura mater, while the cortical depth probes **130** are below the dura mater. In alternative surgical procedures the planar component of the neurological surface probe **101** is below the dura mater, requiring the formation of a flap of the dura mater during the surgery. Regardless of the formation of a dural flap during the surgery, in most procedures, the cortical depth probes **130** are subdural, and the microelectrode elements **140** are intended to be in contact with several cortical layers **201**.

In some embodiments, selectable microelectrode elements **140** can be activated to record from the neurological target **200**. Additionally, recordings of neurological activity from microelectrode elements **140** can be used to identify the location or position of the microelectrode element **140**. For example, a microelectrode element **140** that is recording from cortical layer **201***a* will have a different signal than a microelement **140** that is recording from cortical layer **201***b*. As an additional example, a microelectrode element **140** that is recording from cortical layer **201***b* will have a different signal than a microelement **140** that is recording from cortical layer **201***c*. In this manner, the physician can determine the positioning of the microelectrode elements **140**, and the neurological surface probe **101** in the neurological target **200**.

In some embodiments, the microelectrode elements **140** that are used to record from the cortical surface **221** and cortical layers **201** are particularly useful in the diagnosis of epilepsy. The recorded activity in the patient can be used to determine the electrophysiological origin of an epileptic seizure, and can help the physician decide corrective or surgical action to be taken. In many cases the surgeon may recommend a surgical resection. If performed with this device, the precision of the resection may be improved and lead to better clinical outcomes. Additionally, if the resection is more precise, the patient may be able to keep additional neurological functionality that could have been lost to a larger resected area.

In some embodiments, selectable microelectrode elements **140** can be activated to stimulate a neurological target **200**. Additionally, functional outcome of the neural stimulation can be used to identify the location or position of the microelectrode element **140** by a clinical evaluation of the patient undergoing the stimulation. For example, a microelectrode element **140** that is stimulating a cortical layer **201** in the motor cortex responsible for right hand index finger movement will experience twitching and or movement in their right hand index finger. As an additional example, a microelectrode element **140** that is stimulating in a cortical layer **201** in the auditory lobe may experience the perception of sounds. As an additional example, a microelectrode element **140** that is stimulating in a cortical layer **201** in the visual cortex may

experience the perception of sight. In this manner, the physician can determine the positioning of the microelectrode elements **140**, and the neurological surface probe **101** in the neurological target **200**.

In some embodiments, the microelectrode elements **140** that are used to stimulate the cortical surface **221** and cortical layers **201** are particularly useful in the treatment of stroke. The stimulation may not create a functional outcome such as movement of limbs, but may improve the ease with which patients can move. This stimulation applied to the microelectrode element **140** may be sub-threshold stimulation, meaning that it will not generate action potentials in neurons, but facilitate the ability of a neuron to reach the action potential threshold, by altering the extracellular potential.

In some embodiments, the microelectrode elements **140** that are used to stimulate the cortical surface **221** and cortical layers **201** are particularly useful in the treatment of chronic pain. The stimulation can be applied to a region of the sensor cortex where the physician has concluded that the region may be linked to the patient's pain. For example, a patient that presents himself with chronic pain in the face can implanted with the device in the general region governing sensation of the face in the sensory cortex. This stimulation can be applied to the microelectrode element **140** to suppress pathological activity in order to treat the pain.

Referring now to FIG. **4**, a schematic of the cortical neuromodulation device **100** is provided. The schematic begins with an external controller **170** which the operator can use to functions in the device. The external controller **170** can be in direct electrical contact with the control circuitry **160**, or wirelessly connected through antenna circuitry. The control circuitry **160** is used to translate the commands from the external controller **170** to stimulate and or record from the device. The control circuitry **160** is also used to transmit captured information from the device to the external controller **170** for display or processing. Subsequently the control circuitry is electrical communication with the neurological surface probe **101**. The communication is preferably through a tether wire or ribbon cable (not shown). Protruding from the neurological surface probe **101** are the cortical depth probes **130***a* through **130***n* (collectively **130**), where n is an arbitrary quantity. Furthermore, each cortical depth probe **130** incorporates at least one microelectrode elements **140**.

Referring now to FIG. **5**A, a top view of the exemplary embodiment in FIG. **1** is provided. FIG. **5**B is a detailed planar view of the control module **150**. The image demonstrates the curvature of the upper housing **152**, and the shape of the lower housing **151**. In particular, the fixation structures **156** are designed in order to be slightly offset from the planar surface of the lower housing **151** in order to be adaptable to all skull shapes, curvatures and sizes.

Referring now to FIG. **6**B, an additional perspective view of the neurological surface probe **101** is provided. In the image, cortical depth probes **130***a* through **130***c* are the most proximal. In FIG. **6**C, a perspective view of the neurological surface probe **101** is demonstrated where currents have been applied to a selection of microelectrodes **140**. Microelectrodes that have a cathodal signal applied to them are labeled **140**NEG collectively. Microelectrodes that serve as electrical ground are label **140**GND collectively. FIG. **6**D demonstrates the electric field isosurfaces **141** that the applied currents would create. It is understood by those skilled in the art that any combination of signals (anodal, cathodal, ground) can be applied to any combination of microelectrodes **140** in order to create an arbitrary, or intentionally designed, three-dimensional electrical field in the tissue volume where the neurological surface probe **101** has been implanted.

Referring now to FIG. **6**B, an additional perspective view of the neurological surface probe **101** is provided. In the image, cortical depth probes **130***a* through **130***c* are the most proximal.

Referring now to FIG. **7**A, a frontal planar view of the neurological surface probe **101** is provided. In the image cortical depth probes **130***g* through **130***i* are shown. On cortical depth electrode **130***i*, the microelectrode elements **140** are labeled, **140***ia* through **140***id*. The microelectrode element **140***ia* is most proximal along the cortical depth probe **130***i* to the planar surface of the neurological surface probe **101**. The microelectrode element **140***id* is most distal along the cortical depth probe **130***i* to the planar surface of the neurological surface probe **101**.

Referring now to FIG. **7**B and FIG. **7**C, two additional planar views of the neurological surface probe **101** are provided. In the image cortical depth probes **130***c*, **130***f*, and **130***i* are shown. In FIG. **7**B the cortical depth probe **130***c* is the proximal, whereas the cortical depth probe **130***i* is the most distal.

In FIG. **8**A, a detailed perspective view of one cortical depth probe **130***g* is provided. In FIG. **8**B an additional detailed perspective view of one cortical depth probe **130***g* is provided. The microelectrode elements on the surface of the cortical depth probe **130***g* are labeled **140***ga* through **140***gd*.

FIG. **9** partially demonstrates how the assembly of the neurological surface probe is performed. Additionally, in this example, the cortical depth probes **130** have not yet been bent down to protrude from the surface of the neurological surface probe **101**. The supportive backing layer **120** has been constructed as described above. On its surface are cutouts of the structure that will create the cortical depth probe **130** which is here referred to as a cortical depth probe backing **132**. Likewise, on the microelectrode array film **110**, a structure referred to as the cortical depth probe film **135** is implemented. In this exemplary embodiment, there are nine cortical depth probe backings **132** and nine cortical depth probe films **135**.

By a process of bonding, the microelectrode array film **110** is attached to its supportive backing layer **120**. FIG. **10** demonstrates the assembled neurological surface probe **101** after bonding, but before the cortical depth probes **130** have been bent down to protrude from the planar surface of the neurological surface probe **101**.

In use, the cortical neuromodulation device **100** is placed surgically through a craniotomy formed in the skull. FIG. **11**A is a perspective view of the placement of the device. The image demonstrates a cross section of the brain surface **220** and skull **225**. A circular craniotomy **226** has been performed in the skull. The neurological surface probe **101** has been surgically placed, with its cortical depth probes **130** piercing the dura mater (not detailed) and positioned subdurally. The control module **150** is placed on a different section of anatomy. It is surgically placed on the surface of the skull **225** and can be fastened using cranial screws. FIG. **11**B demonstrates an additional perspective view of the cut-away anatomical region. FIG. **11**C demonstrates an additional planar side view of the cut-away anatomical region.

In some embodiments, it is preferable to integrate the control module with the neurological surface probe into one device, and avoid a wire or ribbon cable tether. The additional embodiment of an integrated cortical neuromodulation device **300** in FIG. **12** demonstrates the integration of all system components into one module.

FIG. **13** demonstrates an additional perspective view of the alternative embodiment. In some embodiments, the control circuitry **360** can be directly implemented on the microelec-

trode array film **310**. Additionally, in some embodiments, the loop antenna **365** can be implemented on the microelectrode array film **310**.

FIG. **14** demonstrates a planar view of the integrated cortical neuromodulation device **300**. The cortical depth probes **330** and their respective microelectrode elements **340** protrude from the lower surface of the device.

In use, the integrated cortical neuromodulation device **300** is placed surgically through a craniotomy formed in the skull. FIG. **15** is a perspective view of the placement of the device. The image demonstrates a cross section of the brain surface **321** and skull **325**. A circular craniotomy **326** has been performed in the skull. The integrated cortical neuromodulation device **300** has been surgically placed through the craniotomy, with its cortical depth probes **330** piercing the dura mater (not detailed) and positioned subdurally. FIG. **16** provides an additional planar view of the placement of the device in a cross section of human anatomy.

In some embodiments, it is preferable to have a circular neurological surface probe. FIG. **17**A demonstrates a perspective view of a circular neurological surface probe **401**. The device incorporates four cortical depth probes **430**. On each cortical depth probe **430** a linear array of microelectrode elements **440** is implemented. Additionally, a large surface electrode **430**, generally of diameter 3 mm, is used to record EEG signals from the surface of the brain. Finally, a ribbon cable tether **480** is used to communicate the microelectrode elements **440** to a control module (not shown) as described in previous embodiments. FIG. **17**B demonstrates an additional perspective view of the circular neurological surface probe **401**. In FIG. **17**C, a perspective view of the circular neurological surface probe **401** is demonstrated where currents have been applied to a selection of microelectrodes **440**. Microelectrodes that have a cathodal signal applied to them are labeled **440**NEG collectively. Microelectrodes that serve as electrical ground are label **440**GND collectively. FIG. **17**D demonstrates the electric field isosurfaces **441** that the applied currents would create. It is understood by those skilled in the art that any combination of signals (anodal, cathodal, ground) can be applied to any combination of microelectrodes **440** in order to create an arbitrary, or intentionally designed, three-dimensional electrical field in the tissue volume where the circular neurological surface probe **401** has been implanted.

The circular neurological surface probe **401** is implemented by combining a supportive backing layer with a microelectrode array film. FIG. **18**A demonstrates an exemplary circular supportive backing layer **420**. It consists of a planar central body from which four cortical depth probe backings **432** protrude. Additionally, at the base of each cortical depth probe backings **432** are bending slits **433** that facilitate the bending of the probe into its final three-dimensional construction. FIG. **18**B demonstrates the circular microelectrode array film **410** that is used in the current embodiment. It consists of four cortical depth probe film **435** on which the microelectrode elements **440** are disposed. The circular supportive backing layer **420** and the circular microelectrode array film **410** are bonded in a process that attaches them to each other. Subsequently, the cortical depth probes **430** are bent into place.

In some embodiments, it is preferable for a circular neurological surface probe to have a central cortical depth probe. FIG. **18**C demonstrates an additional embodiment of a circular supportive backing layer **420**C with an additional central cortical depth probe backing **432**CM. It consists of a planar central body from which four cortical depth probe backings **432**C protrude, and a central cortical depth probe backing **432**CM of the same length and dimensions projects from the center of the circular supportive backing layer **420**C. Additionally, at the base of each cortical depth probe backings **432**C are bending slits **433**C that facilitate the bending of the probe into its final three-dimensional construction. Additionally, at the base of the central cortical depth probe backing **432**CM are bending slits **433**CM that facilitate the bending of the central probe into its final three-dimensional construction.

FIG. **18**D demonstrates the circular microelectrode array film **410**C that is used in the current embodiment. It consists of four cortical depth probe films **435**C on which the microelectrode elements **440**C are disposed. Additionally, a central cortical depth probe film **434**CM of the same length and dimensions projects from the center of the circular microelectrode array film **410**C. The circular supportive backing layer **420**C and the circular microelectrode array film **410**C are bonded in a process that attaches them to each other. Subsequently, the cortical depth probes are bent into place, with the central cortical depth probe taking a position that is normal to the plane formed by the planar section of the supportive backing layer **420**C.

Referring now to FIG. **18**E, a perspective view of the circular neurological surface probe with central pin **401**C is demonstrated. The components demonstrated in FIG. **18**C and FIG. **18**D are assembled to implement this embodiment. It consists of four cortical depth probes **430**C and a central cortical depth probe **430**CM. Microelectrode elements **440**C are disposed on all five cortical depth probes. The central cortical depth probe **430**CM of the same length and dimensions as the cortical depth probes **430**C project from the center of the circular neurological surface probe **401**C surface. The circular supportive backing layer **420**C and the circular microelectrode array film **410**C are bonded in a process that attaches them to each other. Subsequently, the cortical depth probes are bent into place, with the central cortical depth probe taking a position that is normal to the plane formed by the planar section of the supportive backing layer **420**C.

Referring now to FIG. **19**A a cross-sectional view of a portion of human brain anatomy **421** is shown, illustrating the exemplary circular neurological surface probe **401** positioned at a neurological target **422**. In general, circular neurological surface probe **401** is representative of any of the cortical neuromodulation devices described herein. The circular neurological surface probe **401** includes an array of microelectrode elements along its individual cortical depth probes. Preferably, circular neurological surface probe **401** is implanted using by performing craniotomy. Its ribbon cable tether **480** remains outside of the human body, while the circular neurological surface probe **401** is implanted on the surface of the cortex of the brain. As in other embodiments, individual cortical depth probes are meant to be implanted subdurally, with the microelectrode elements in contact with at least one of the subdural layers of the cortex.

Referring now to FIG. **19**B, a planar view of the positioning of the exemplary circular neurological surface probe **401** in a portion of human brain anatomy **421** referred to as the neurological target **422**. As illustrated, one or more of the microelectrode elements circular neurological surface probe **401** are positioned in intimate contact with the neurological target **422**. One or more additional microelectrode elements of the circular neurological surface probe **401** may reside at locations not in the immediate vicinity of the neurological target **422**. In at least some embodiments, one or more of the microelectrode elements are remotely accessible from a proximal end of the circular neurological surface probe **401** via one or more electrically conductive leads (not shown).

In some surgical procedures it would be highly beneficial to the patient to have several circular neurological surface probes **401** implanted in the region of the neurological target **422**K. FIG. **20**A demonstrates a cross-sectional view of a portion of human brain anatomy **421**K, illustrating four exemplary circular neurological surface probes **401**K positioned at a neurological target **422**K. FIG. **20**B is a more detailed close-up view of the neurological target **422**K. Four circular neurological surface probes **401**Ka, **401**Kb, **401**Kc, **401**Kd (collectively **401**K) were implanted in the neurological target **422**K. It is highly beneficial in some surgical procedures to avoid the sulci **405**K on the surface of the brain. The sulci **405**K are regions where the brain surface folds and may be highly vascularized. The circular neurological surface probes **401**K each have a ribbon cable tether, collectively **480**K, that can lead to the external portion of the patient.

In practice the physician will determine how many circular neurological surface probes **401**K should be implanted. In some cases, it might be beneficial to implant only one, as the physician might determine that this will provide enough physiological information, or enough of a therapeutic stimulation volume. In some cases, it will be beneficial to implant a multiplicity of circular neurological surface probes **401** in the region, in order to increase the probability of finding the neurological target. The decision to implant a certain quantity of devices may be taken before the surgery, using surgical planning software. Alternatively, or in addition, the decision can be taken during the surgery.

In some embodiments, it is preferable to integrate the control module with the circular neurological surface probe into one device, and avoid a wire or ribbon cable tether. The additional embodiment of an integrated circular cortical neuromodulation device **401**M in FIG. **21**A demonstrates the integration of all system components into one module. The device incorporates four cortical depth probes **430**M. On each cortical depth probe **430**M a linear array of microelectrode elements **440**M is implemented. Additionally, a lower housing **451**M for control module is implemented directly above the planar region of the circular supportive backing layer **420**M. The upper housing **452**M is intended to encapsulate the control circuitry **460**M and loop antenna **465**M which are used to control and transmit information to the integrated circular cortical neuromodulation device **401**M. On the surface of the circular microelectrode array film **440**M are microelectrode array elements **440**M which are in communication with the control circuitry **460**M through embedded conductive traces (not shown). FIG. **21**B demonstrates an additional perspective view of the integrated circular neurological surface probe **401**M. In this image, the implementation of an EEG electrode **441**M of 3 mm diameter is visible. FIG. **21**C is an additional planar view of the exemplary integrated circular cortical neuromodulation device **401**M.

Referring now to FIG. **22**, a perspective view of a human brain anatomy **421**M is shown with the exemplary embodiment of the integrated circular cortical neuromodulation device **401**M implanted in a neurological target **422**M. In this exemplary embodiment, the connection of a ribbon cable tether the external portion of the patient is not necessary. However, an external control module (not shown) is required to communicate with the implanted device. FIG. **23** demonstrates a more detailed view of the portion of human anatomy **421**M and the positioning of the exemplary circular neurological surface probe **401**M in the neurological target **422**M.

In some surgical procedures, it would be highly beneficial to the patient to have several integrated circular neurological surface probes **401**M implanted in the region of the neurological target **422**M. FIG. **24** is a close-up perspective view of a portion of human brain anatomy **421**M, illustrating five exemplary integrated circular neurological surface probes **401**Ma, **401**Mb, **401**Mc, **401**Md, **401**Me (collectively **401**M) positioned at a neurological target **422**M. It is highly beneficial in some surgical procedures to avoid the sulci **405**M on the surface of the brain. The sulci **405**M are regions where the brain surface folds and may be highly vascularized. The integrated circular neurological surface probes **401**M can wirelessly communicate to the external portion of the patient.

In all of the embodiments presented, it is understood that the devices are meant to be implanted using a surgical procedure on the surface of the brain. Additionally, it is intended that the cortical depth probes which protrude from all embodiments are meant to be in the subdural region or the brain, and the microelectrode elements on the surface of the cortical depth probes are meant to be in contact with at least one of the cortical layers. The neurological surface probes are placed on the brain generally for recording and/or stimulation of the cortex. The region of the cortex that the physician is target for diagnosis or therapy is termed the neurological target.

The microelectrode elements can also be placed in other parts of the body, such as the retina, the peripheral nervous system for neural recording and/or neural stimulation of such portions of an animal anatomy. Although microelectrodes are discussed generally throughout the various embodiments, there is no intention to limit the upper or lower size of the microelectrodes. The devices and methods described herein are generally scalable, with a microelectrode size determined according to the intended application. For at least some of the neurological applications, microelectrodes are dimensioned sub-millimeter. In some embodiments, microelectrodes are dimensioned sub-micron. In some embodiments, the microelectrodes are formed as planar structures having a diameter of about 50 μm that are arranged in a linear array with center to center spacing of about 100 μm. The planar structure of the microelectrodes can have regular shapes, such as circles, ellipses, polygons, irregular shapes, or a combination of such regular and/or irregular shapes.

FIG. **23**A is a schematic diagram of one embodiment of a cortical depth probe assembly. The microelectrode tip assembly **500** includes a supporting member **502** including an elongated portion terminating in a distal tip **506** and a proximal extension **510**. A linear array of three microelectrode elements **504** is arranged along a longitudinal axis of the elongated portion of the support member **502**. A corresponding number of three electrode contacts **508** are located on the proximal extension **510**. Each microelectrode element of the array **504** is interconnected to a respective one of the electrode contacts **508** through a respective electrically conducting lead trace **512**. In the exemplary embodiment, a polymer layer **514** is applied to at least one surface of the underlying support member **502**. Each of the microelectrode leads, electrode contacts **508**, and interconnecting lead traces **512** is implemented as an electrically conducting layer on or within the polymer layer **514**. Although a linear array of microelectrode elements is shown, other embodiments are possible with non-linear, planar, curved surface, and volumetric (i.e., three-dimensional) distributions of such microelectrodes are possible.

Fabrication Methods

There are several techniques to achieve the microfabricated component and the required mechanical and electrical characteristics. The fabrication procedure is a series of procedural steps in which various layers are deposited or removed (e.g., etched) to achieve a final form. Exemplary sequence of procedural steps is described herein.

Step 1: The Carrier Wafer and Sacrificial Layer

In a first step illustrated in FIG. **23**A, a carrier substrate **650** is provided, such as a wafer composed of a crystalline material, such as Silicon, or an amorphous material, such as glass, in particular a thermal shock resistant borosilicate glass commercially available under the brand name PYREX®, or other suitable smooth supportive material. A first layer **652** comprising at least two sub-layers is applied to a surface of the wafer **650**. One of the sub-layers **652** is a sacrificial layer deposited on the wafer **650**, which will be removed in a subsequent electrochemical etch step. Preferably, the sacrificial sub-layer is preceded by another sub-layer, referred to as an underlayer, that will serve to form the electrochemical cell required to etch the sacrificial layer. In the preferred embodiment, the sacrificial sub-layer is Aluminum, or an alloy of Aluminum such as AlSi, which has a smaller granularity, whereas the underlayer is a TiW alloy, Chrome, or similar metal. The sacrificial layer is represented as a black line **652** in the image below, the carrier wafer **650** is shown in gray. Each of the images illustrated in this series represents a cross section of an exemplary embodiment, and are used herein to describe the procedural steps.

In some embodiments, the sacrificial layer **652**, in addition to facilitating electrochemical removal of the finished device, is to establish a granularity, or grain size to the surface of the finished device. Namely, the sacrificial layer can add a micro or nano-roughness to the surface that can be precisely controlled at least in part by the selection of a suitable underlayer. For example, Aluminum can be deposited by DC Sputtering with a grain size ranging from 5 nm or less to 600 nm or more. This grain size provides a first grainy surface. A polymeric layer is subsequently deposited over the grainy sacrificial layer. This polymeric layer can be locally etched in order to create vias that open onto the grainy sacrificial layer. Subsequently, a metal layer is deposited over the resulting grainy surface, and polymeric layer, in which the deposited metal serves as the neuro-recording/stimulation microelectrode element, and wire trace. The area of the metal that falls into the via in the polymeric layer forms the microelectrode surface. The area of the metal falls on the polymeric layer can be etched into linear traces and form the interconnect between microelectrodes and bond pads or circuitry. The process is described below as a "backside microelectrode." Due to such an increase in granularity over a relatively flat surface, the overall surface area of the metal layer will have a higher effective surface area than that area subtended by the perimeter of the element. Beneficially, the increased surface area results in a corresponding decrease in electrical impedance of the electrode element. This concept is important in that it facilitates recording, allowing a greater recording fidelity with less complexity due to the reduction in impedance, while maintaining the same small diameter that guarantees high localization of the neural activity. An electrically conducting surface of an exemplary microelectrode element thus formed is illustrated in the image of FIG. **30**.

Step 2: Deposition of First Polymeric Layer

Referring to FIG. **25**B, the next step in the fabrication process includes depositing a first polymeric layer **654**—sometimes referred to as a resin layer **654**. The first polymeric layer **654** can be deposited upon the sacrificial layer **652**. This can be done by any suitable means known to those skilled in the art of MEMS processing, by: (i) spin coating a liquid polymer precursor such as Polyimide or Silicone precursor; (ii) depositing a polymer through chemical vapor deposition as is done with parylene-C; or (iii) laminating a polymer sheet **654** onto the wafer **650**. In some embodiments, the polymer layer **654** is heated, or baked, to polymerize.

Referring next to FIG. **25**C and FIG. **25**D, an optional step includes etching of first polymeric layer **654**, as may be beneficial when preparing a device having one or more backside electrodes, that will ultimately be located along an underside of the finished device. In this optional step, the first polymeric layer **654** is locally etched in order to form open areas **652**, where metals for such backside microelectrodes may be later deposited. This step is optional, and unnecessary when there is no need for any such backside electrodes on the finished device—all microelectrode contacts being formed on a front surface of the finished device. This step is also advantageous, because the backside electrode metal layer, when included, will also benefit from the higher effective surface area that can be gained from the sacrificial layer's granularity.

The etching can be performed by depositing a mask **656** on the first polymeric layer **654**. Using well established methods for thin film processing, the mask **656** can be photolithographically defined. For example, a photosensitive resin **656** is spin coated onto the polymeric layer **654**. A process of exposing an unmasked portion of the resin layer **657** to UV light is used for those areas in which the operator chooses to remove the polymer layer **654**. The device is developed in a solvent that will selectively remove only the unmasked areas **657** that were exposed to UV light. This selective etching process locally opens areas of the polymeric layer **654**, by etching, exposing in this instance the underlayer **652**. In some embodiments, the device is etched in oxygen plasma to remove the exposed portion of the polymeric layer **657**. The etch mask **656** may also be removed by the same etching process, but if it is thicker than the polymer layer it may not be completely removed. Illustrated in the figures is a defined etch mask **656**. Alternatively or in addition, the etch mask **656** can also be implemented in a non-photodefinable layer, such as Silicon Dioxide deposited by DC Sputtering. The Silicon Dioxide then has the photoresist deposited and photolithographically defined on top of it. After etching the polymeric layer **654**, the Silicon Dioxide mask can be optionally removed.

FIG. **25**D illustrates the device after the exposed portion of the polymer layer **657** was removed. As illustrated, a portion of the sacrificial layer **652** is now exposed. In some embodiments, the photoresist mask **656** cab be subsequently removed using a suitable solvent.

Step 3: Deposition and Definition of Metal Layer

The deposition of the layer can also be made through a resist mask **670**, as shown in FIG. **25**G. In this case a photoresist mask **686'** would be photolithographically defined on the polymer layer **654**. An electrically conductive (e.g., metal) layer **692'** can then be deposited over the masked device. Thus, unmasked areas **687** at which it is desirable to have an electrically conducting layer **690** formed, are open with respect to the photoresist mask **686'**, such that the a portion of the deposited electrically conductive layer **692'** lands directly onto the polymeric layer **654** at the unmasked area **687**. This technique is sometimes referred to as a "lift off" technique. The photoresist mask **686'**, with any electrically conductive layer **692'** thereon, is then dissolved, such that the only remaining metal **690** is on the polymer at the formerly unmasked areas. Note that the metal layer **692'** on top of the photoresist **686'** is also removed by removal of the photoresist mask **686'**. Beneficially, that portion of the electrically conducting layer **690** in contact with the polymeric layer **654** remains after removal of the mask **686'**.

In an alternative method, referring now to FIG. **25**H, a metal layer **692"** can be deposited onto the entire surface of a wafer **650**. As illustrated, the metal layer **692"** is provided on

top of the polymeric layer **654**, which is provided on top of the sacrificial layer **652**. A masking layer **686"** is provided over that portion of the metal layer **692"** to remain. Exposed regions of the metal layer **692"** can then be removed locally by a photolithographic step such as demonstrated below.

Referring next to FIG. **25**E, an electrically conductive layer that serves as the electrode **680** and one or more electrically conductive traces **682** is next deposited. Such an electrically conductive layer can include a metal layer deposited by any suitable thin-film process, such as DC sputtering, RF Sputtering, or evaporation techniques. The metal deposited in the electrically conductive layer **680**, **682** is preferably platinum, iridium, platinum-iridium alloy, iridium-oxide, titanium, or a titanium alloy to ensure acceptable electrical characteristics (such as charge transfer) and mechanical strength.

In a preferred embodiment, the metal layer **680**, **682** is deposited with an adhesion promotion layer in contact with the polymer. For example, titanium can be sputtered onto the polyimide layer **654** in an initial partial step to improve adhesion, followed by a platinum layer deposited in an intermediate partial step, and optionally, a titanium layer may them be deposited onto the platinum layer in a subsequent partial step. This creates a Ti—Pt—Ti sandwich, where the titanium is responsible for adhering the platinum to the polyimide on either side of it, and the platinum is the metal layer that will be used.

For embodiments that produce backside electrodes, as described above in reference to FIG. **25**C through FIG. **25**E, then the electrically conductive layer **680** will be in contact with the sacrificial layer **652** in the region of the backside electrode **680**. The metal deposition technique is selected to ensure that there is contact between the metal on top of the polymeric layer **654**, and the metal on the exposed portion of the sacrificial layer **652**. This is done by ensuring the metal **680** is conformally deposited, and that the polymeric layer **654** is not too thick. The metal layer **680** can then be photolithographically defined as explained above. An etch in a plasma, such as Chlorine gas plasma, can be used to remove the metal layers deposited using a photoresist mask. The photoresist mask can then be removed in a solvent.

Step 4: Deposition of 2nd Polymeric Layer

Referring next to FIG. **25**I for a backside electrode embodiment and FIG. **25**H, a second polymeric layer **672**, **692** is deposited using a suitable technique, such as any of the techniques described above with respect to FIG. **25**B. The second polymeric layer **672**, **692** is deposited onto the underlying polymeric layer **654**, **664**, and any exposed metal layer **658**, **668**. In some embodiments, the first polymeric layer **654**, **664** can be processed in order to increase its adhesion to the second polymeric layer **672**, **692**. For example, such processing can be accomplished through surface roughening or chemical alteration using an oxygen plasma. The second insulative, or polymeric layer **672**, **692** isolates the electrical traces, when formed on different layers with respect to each other. In some embodiments, the polymeric material can be subjected to thermal process, such as baking.

Step 5: Definition of Polymeric Layers

Referring next to FIG. **25**I through FIG. **25**K, to define the one or more polymer layers **654**, **691** and therefore the device itself, an etch mask **695** is deposited to an external surface of the device. This etch mask **695** may consist of a photodefinable resist but preferably it will be a hard etch mask such as silicon dioxide or amorphous silicon which can withstand the etch of the polymeric layer without significant degradation.

The wafer **650** at this point also has a hard mask **693** deposited, for example, by DC or RF sputtering. A photodefinable **695** resist is deposited on the hard mask **693** and the areas of the polymer **654**, **691** that are to be etched are defined.

The hard mask **693** is then etched with a different gas then would be used to etch the polymeric layer **654**, **691**, for example CF4 plasma. Now the one or more polymeric layer **654**, **691** can be etched with a gas, such as oxygen plasma, to the sacrificial layer **652**, as shown. Thus, the remaining portions of the hard mask shown in FIG. **25**K define the extent of the device, by defining the device's edges **659**.

The remaining portions of the hard mask **693** can be optionally removed in a subsequent step. The goal of this etching process is to: (i) define the microelectrode sites; (ii) define the device shape; and (iii) define the contact areas for electronics or wire attachment. A top view of an exemplary finished microelectrode device is shown in FIG. **31**. A cross-section of another exemplary finished microelectrode device is shown in FIG. **32**.

If the option of making backside electrodes is taken in step 2, the device will have microelectrodes at its surface once removed from the substrate.

Step 6: Optional Bonding of Electronics

If the device is to be integrated with electronics, referring now to FIG. **25**L, the contact pads **699** can be used at this point to connect to an electrical circuit device **697**. For example, an Integrated Circuit chip **697** can be connected to the contacts **690** (FIG. **25**K) by flip-chip bonding the chip **697** to the device **661**, using a conductive epoxy interlayer. The chip **697** can then be further attached by chemical bonding, such as an epoxy to ensure a strong and reliable connection to the device **661**.

Step 7: Removal of Devices from Carrier Wafer

A final step of the fabrication process is illustrated in FIG. **25**M, to remove the device **661**, such as a MEMS device, from the underlying wafer **650**. The sacrificial layer **652** (e.g., FIG. **25**L) is electrochemically etched away. Removal of the sacrificial layer **652** from under the device **661**, frees the underside of the device **661** from the wafer **650**. This can be accomplished by placing the wafer in a saline bath with a high NaCl concentration. A platinum electrode in the bath can be used as a reference. A voltage is applied to the aluminum layer with respect to the platinum electrode. The electrochemical cell created by the Aluminum and TiW etches the aluminum, and this etch continues below the devices. The devices fall into the bath and are removed.

FIG. **26** is a micrograph of an embodiment of a backside microelectrode element **700**. The image is taken at the process step shown in FIG. **25**E. The granularity **702** of the aluminum sacrificial layer surface **704** is used to increase the effective surface area of a metal electrode in a subsequent step. Also shown is a portion of an interconnecting lead **706** in electrical communication with the microelectrode element **700**.

FIG. **27** is a planar view of a construction element of an embodiment of a microelectrode tip. The construction element includes a stencil frame tree **640** including eight rigid backing members **642** releasably attached to a supporting construction frame **644**. Each of the rigid backing members **642** includes an elongated portion, and an proximal portion having an opening **646** to accommodate one or more electronic devices, when fabricated. The stencil frame tree **640** can be implemented in a rigid material, such that each of the individual supporting construction frames can be bonded to the devices on the carrier wafer.

FIG. **28** is a schematic view of a portion of the construction element illustrated in FIG. **29**, illustrating a close up of the

assembled components. In this exemplary embodiment, the polymer devices were fabricated using a "backside" electrodes process

FIG. **29** illustrates an exploded schematic view of a construction element of an embodiment of a microelectrode array tip. The stencil frame tree **400** is placed on a surface of a carrier wafer including micro-array devices **649** formed therein. The stencil frame tree **400** is suitably aligned with the micro-array devices **649** of the carrier wafer **648**, and bonded thereto. One or more electronic devices can be suitably placed on the polymer devices either after or before the stencil frame tree **400** is bonded to the carrier wafer **648**.

FIG. **30** is a schematic view of another portion of the construction element illustrated in FIG. **29**. Once the sacrificial layer has been removed as described above, the devices **649** are released from the carrier wafer **648** and are now bonded to the stencil **640** for support. In the exemplary embodiment, the side of the polymeric device **649** facing the carrier wafer **648** (and in contact with the sacrificial layer) has the microelectrodes at its surface. In general, microelectrodes may be included in either or both sides as described herein.

In some embodiments, a rigid back **642** on the polymer micro-device **649** is required. This renders the device **649** fully, or locally, rigid. This rigidity might be advantageous for insertion into tissue. The concept is a stencil shape **640** which can be bonded onto the devices on the carrier wafer where they have been fabricated. The stencil shape **640** can be implemented in a polymer, such as PEEK or Polyurethane, or in metal such as Medical Grade Stainless Steel or Titanium. It can be molded into shape, cut by machining or laser, or stamped out. When this rigid structure has been attached to the devices, the electronic chip can be bonded. The electronic chip can also be bonded to the devices beforehand. After the assembly process the devices can be removed from the carrier wafer using the same sacrificial etching techniques as described above. A further assembly procedure can be to remove the rigid backing from its frame and integrate the device with its final structure. In some embodiments, the rigid backing is conductive. In other embodiments, the rigid backing is non-conductive. When this support structure is of a conductive material, it can also serve as the electrical ground or reference for the stimulation.

FIG. **33**A through FIG. **36**C are images of additional embodiments, in which one or more backing layers are used to support a microelectrode film. The one or more backing layers can be rigid, or semi-rigid. In some embodiments, the one or more backing layers can be flexible FIG. **33**A illustrates a planar view of a construction element used to create a rectangular array of microelectrode tips. The exemplary construction element includes a stencil frame tree **740'** including an arrangement of, in this example, twelve individual semi-rigid backing members **742**. The stencil frame tree **740'** can include a rigid material, such as medical grade stainless steel. In some embodiments, the stencil frame tree **740'** can be bonded to one or more microelectrode devices, for example, on a carrier wafer.

The stencil frame tree **740'** can be implemented by laser cutting, water-jet cutting, chemical etching using photosensitive masks, or another method used to obtain medical-grade, two-dimensional structures. The stencil frame tree **740'** can include one or more, open-ended or enclosed, apertures **746**, for example, in which microelectronic circuitry can be located.

The stencil frame tree **740'** is also characterized by its overall shape and size. Generally, any overall shape is contemplated, including polygons, ellipses, circles, serpentines, irregular shapes, and any combination of such shapes. In the illustrative embodiment, a substantially rectangular stencil frame tree **740'** is characterized by its width, W, and its length, L. In the exemplary embodiment, the width is 20 mm, and the length is 15 mm. The stencil frame tree **740'** is generally thin to facilitate fabrication and placement within the body. In the exemplary embodiment, the thickness is about 0.1 mm (not shown). Generally, the stencil frame tree **740'** has an overall shape and dimensions conforming to the anatomy for which it is meant to be used. Such target anatomies include any of the anatomies described herein, including the brain, the spine, the peripheral nerve system, the cochlea, the retina, and other parts of the body. In some embodiments, it may have a width as wide as 20 cm or greater, and a length as long as 15 cm or greater, although no general limitation as to size and shape are contemplated.

FIG. **33**B is a perspective view of a portion of the stencil frame tree **740**, illustrating several semi-rigid backing members **742** formed therein. The general shape semi-rigid backing members **742** can be formed by any suitable means, including pushing, molding, or stamping. Once formed, the semi-rigid backing members **742** can be bent or otherwise formed into a downwards position as shown in FIG. **33**C. In other embodiments, the backing members **742** can be bent into an upward position, or into a combination of downward and upward positions. This action results in protruding portions forming a supportive, probe backing member **743**. As mentioned in previous embodiments, this bending can be performed before, or after, a microelectrode film has been attached to the stencil frame tree **740'**.

FIG. **34**A and FIG. **34**B demonstrate additional embodiments of a stencil frame tree **740"**, **740'"** (generally **740**). In some embodiments, the stencil frame tree **740** can include one or more, vertical elongated grooves or openings **745***a* through **745***c* (generally **745**) in order to make the stencil frame tree **740** more flexible along one or more axes, enabling a generally planar structure to conform to a portion of anatomy that is not flat, as shown in FIG. **34**A. In some embodiments, the stencil frame tree **740** can include one or more, horizontal **746** or vertical elongated grooves or openings **745**, in order to make it more flexible along several axes, enabling it to conform to a portion of anatomy which is not flat, as shown in FIG. **34**B.

FIG. **34**C and FIG. **34**D demonstrate various embodiments of semi-rigid backing members **742**, illustrating different shapes and features. FIG. **34**C demonstrates a closer view of the embodiment discussed above, characterized by a relatively sharp tip which can promote easier penetration of tissue, including the dura mater on the surface of the brain. The rigid members **742**, **747** are also characterized by their respective length d measured from a base portion to the tip, that can be implemented to be short, or long enough to reach certain areas of anatomy. In some embodiments, one or more of the semi-rigid backing members **742**, **747** of the same stencil frame tree **740** can have different dimensions and/or different shapes. In some embodiments, e.g., for cranial applications, the length d is generally about 1-4 mm but can be as short as 0.5 mm or less, or as long as several centimeters or greater.

FIG. **34**D illustrates an additional embodiment, characterized by a rounded tip which can prevent chronic injury of tissue after implantation. The rigid member **747** also differs by an aperture, or gap in its base **748** which can improve the ease of bending the member into is final, protruding position. Such a gap **748** can be included in any of the embodiments described herein.

FIG. **35**A illustrates a top perspective view of an assembled microelectrode assembly **750** that can be used for recording

and/or stimulation. In this assembly the rigid stencil frame tree **740'** is supporting a microelectrode film **755** (not shown) on its inferior side. Semi-rigid backing members **742** have been bent downwards to protrude from its inferior side. A microelectronic circuit element **752** is electrically coupled between the microelectrode film and an external device (not shown) through flexible electric conduit member **754**.

FIG. **35**B illustrates in more detail a perspective view of a single rigid backing member **742** from the inferior side of the assembly **750**. The microelectrode film **755** is visible, having been bonded to the inferior side. On the inferior side of the microelectrode film **755** are an arrangement of microelectrode elements **765**. The microelectrode film **755** and microelectrode elements **765** conform to the bent rigid backing member **742**, extending away from the plane of the stencil frame tree **740'**. On the surface of the exemplary embodiment are four microelectrode elements or sites **765**. These sites can also be used for one or more of sensing or recording neural activity, or electrical stimulation, or they can be enabled to stimulate and record from the same site. The number of microelectrode sites **765** of each bent rigid backing member **742** can vary from one or more. In this exemplary embodiment there are four microelectrode stimulation sites **765**. They can also be arranged in other configurations, including any of the configurations described herein, such as a tetrode configuration as will be shown in subsequent embodiments, such as in FIG. **42**A through FIG. **42**D and FIG. **43**F through FIG. **43**G.

FIG. **35**C illustrates a perspective view of an assembled microelectrode recording and stimulation device **780**. In this assembly the rigid stencil frame tree **790** is supporting a microelectrode film **795** on its inferior side. Semi-rigid backing members **792** have been bent downwards to protrude from its inferior side. A microelectronic circuit element **782** brings the microelectrode film into electrical contact with an external device (not shown) through flexible electric conduit member **784**.

FIG. **35**D illustrates a closer perspective view of a single rigid backing member **792** from the inferior side of the assembly **780**. The microelectrode film **795** has been bonded to the superior side of the rigid stencil frame tree **790**. The microelectrode film **795** can be implemented using the micro-fabrication processes described herein, and can be bonded to the rigid stencil frame tree **790** by gluing or heating. On the superior side of the microelectrode film **795** are microelectrode elements **796** and **797** which conform to the bent rigid backing member **792**. On the surface is a relatively large microelectrode stimulation site **796** for stimulating neural activity. Additionally, on the surface is an arrangement of four relatively small microelectrode recording sites **797** arranged in a tetrode configuration used for single neural cell recording. The number of microelectrode stimulation sites **796** on each rigid backing member **792** can vary from one or more. There are further tetrode configuration as will be shown in subsequent embodiments, such as in FIG. **42**A through FIG. **42**D and FIG. **43**F through FIG. **43**G.

FIG. **35**E illustrates a perspective view of the array of protruding microelectrode elements **762** shown in FIG. **35**A. The microelectrode film **755** can be implement using any of the microfabrication procedures previously described. In this exemplary embodiment, the backside fabrication process was used. The microelectrode film **755** can be bonded to the stencil tree frame through gluing or heating.

As shown in FIG. **34**A and FIG. **34**B, it may be necessary to include elongated gaps in the rigid backing frame **740** and the bonded microelectrode film **755** in order for the microelectrode assembly **750** to conform to a portion of anatomy. FIG. **36**A shows a portion of human anatomy, the left hemisphere of the brain **771**. On its cortical surface, an exemplary microelectrode assembly **750** has been placed, which can be used to record and/or stimulate neural activity.

FIG. **36**B illustrates an additional perspective demonstrating both the left hemisphere **771** and the right hemisphere **772** of the brain. The microelectrode assembly **750** has been surgical placed on the cortex, and connected to a separate control system (not shown) through electrical conduit **754**. The separate control system can be located within the body, external to the body, or a combination of internal and external. The device is generally placed by creating a craniotomy. The protruding rigid members **742** can puncture the dura mater (not shown) therefore not requiring its surgical removal. Alternatively or in addition, a surgeon will remove the dura mater, and the protruding members **742** will puncture the cortex with a depth that is determined by the length of the protruding member **742**.

This is demonstrated in more detail in FIG. **36**C, in which an array of 12 protruding members **742** have been inserted into the first layers of the cortex. A microelectronic element **752**, when included, can be used to record, stimulate, or both record and stimulate neural activity on each of the microelectrode sites that have been implemented on each of the protruding members **742**. In some embodiments, one or more of the protruding members **742** can be actuated independently or in one or more groupings to record and/or stimulate a desired region addressable by the device **250**. In general, the microelectrode assembly **750** can be configured with any of microelectrode probe described herein, and used in combination with any of the stimulation and/or recording or sensing devices described herein.

Electronic Components

The electronic components of the device enable: (i) recording of neural activity from the microelectrode array to identify which microelectrode sites are closest to the stimulation region of interest; and (ii) stimulation and modulation of neuronal activity with the microelectrode array and the ability to select which microelectrode sites stimulating.

The electronics can be implemented using discrete components, integrated circuit technology, or a combination of both. A black box design of the electronics is shown below. The electronics can be driven by an existing Implantable Pulse Generator (IPG), but will include a telemetric programming interface to properly condition or route the signal from the IPG to the microelectrode array. An embodiment of the electronic components exists which does not require the IPG.

Mechanical Components

The mechanical components and associated assembly processes serve to house the device in a hermetic and biocompatible manner. They also enable connection to an existing Implantable Pulse Generator or the extra-corporeal control unit. The extra-corporeal unit provides power, programming ability and retrieval of information. It can be implanted much like the external cochlear stimulation systems that exist today. In an embodiment that includes an Implantable Pulse Generator, it would serve to retrieve information and program the electrical unit to route the signals from the IPG to the microelectrode array.

Referring to FIG. **37**, a functional block diagram of an exemplary embodiment of a neurological target stimulator **820** configured in a stimulation mode. The stimulator **820** includes an implantable portion **822** including a microelectrode array **826** positionable at a neurological target. The implantable portion **822** also includes a signal generation device **828** for actively stimulating the neurological target. In some embodiments, each of the one or more microelectrodes

of the microelectrode array **826** is in communication with a dedicated signal generation device **828**. The respective stimulation signal provided at an optimized frequency for each individual microelectrode-tissue interface, based on a peak resistance frequency. The implantable portion **822** can include a power source **832**, such as a battery. In some embodiments, the implantable portion **822** also includes a telemetry and control module **834** configured for external communication with an extra-corporeal unit **824**. Such a feature can be used to provide extra-corporeal control for operating the implantable portion **822**.

Referring to FIG. **37**, a functional block diagram of another exemplary embodiment of a neurological target stimulator **840** is illustrated configured in so-called routing mode. The stimulator **840** includes an implantable portion **842** including a microelectrode array **846** positionable at a neurological target. The implantable portion **842** also includes a signal routing circuit **850** configured to direct a stimulation signal to one or more of the microelectrodes **846** for actively stimulating the neurological target. In this embodiment, the stimulation signal is obtained from a separate, implantable pulse generator **857**. The pulse generator **857** is in communication with the implantable portion **842** through an interconnection cable **856** containing one or more signal leads. The implantable portion **842** also includes at least one signal conditioner **848** configured to condition an output signal from the pulse generator **857** suitable for stimulation of the neurological target through one or more of the microelectrodes **846**. The implantable portion **232** generally includes a power source **852**, such as a battery. In some embodiments, the implantable portion **842** also includes a telemetry and control module **854** configured to communicate with an extra-corporeal unit **844**, to provide controls for operating the implantable portion **842**.

Filtering of an Existing Signal.

In some embodiments, the signal conditioner **848** include a filtering circuit to pre-filter or gain adjust (e.g., pre-amplify and/or attenuate) or otherwise condition an existing signal before routing it to a microelectrode array. Several popular filter options include digital filters, such as infinite impulse response (IIR) filters, electronic filters using one or more electrical components, such as inductors and capacitors, and surface acoustic wave (SAW) devices. The filters can be designed through well known filter synthesis techniques to have a preferred performance features. Some of the controllable features in filter synthesis include filtration bandwidth, corner frequency, pass-band ripple, and relative sideband level. Such filters include categories referred to as Butterworth, Chebyshev 1 and 2, and Elliptic filters. The particular implementation—whether analog or digital, passive or active, makes little difference as the output from any implementation would still match the desired output.

FIG. **39** is a functional block diagram of another embodiment of a neurological microelectrode target stimulator **814** is shown. The stimulator **814** includes a microelectrode array **815** positionable at a neurological target of interest. The stimulator **814** also includes an impedance analyzer **816** configured for measuring an electrical impedance, a preferred frequency detector **817**, and a stimulator **818** for electrically stimulating the neurological target.

The impedance analyzer **816** can use any of various known techniques for measuring electrical impedance. Generally, the impedance analyzer **816** provides a test electrical signal having known or measurable attributes to the microelectrode-tissue interface. Such attributes include a voltage level of a voltage source, or a current level of a current source. The test voltage or current, as the case may be, when applied to the microelectrode-tissue interface, induces a sensed current or voltage according to physical properties of the microelectrode-tissue interface. The impedance analyzer **816** can form a ratio of the test signal to the sensed signal, yielding an impedance value according to Ohm's Law: $Z=V/I$. As the microelectrode-tissue impedance Z is a complex quantity, each of the test and sensed electrical signals is identified as having both a magnitude and a phase.

In operation, the impedance analyzer measures a complex impedance of the microelectrode-tissue interface surrounding the at least one microelectrode **815**. The impedance analyzer repeats the measurements at multiple different frequencies, by varying frequency of the applied test electrical signal. Preferably, the multiple frequencies span a frequency range that includes biologically relevant frequencies. The preferred frequency detector **817** identifies the measured impedance being closest to a pure resistance. Such a determination can be accomplished by identifying the measured impedance value having a phase value closest to zero. For example, a measured impedance can be identified having minimum absolute value phase (i.e., $\mathrm{MIN}|\angle Z|$). Such a determination can also be accomplished by identifying the measured impedance value having a minimum reactance (i.e., $\mathrm{MIN}(\mathrm{Im}\{Z\})$). The frequency at which the impedance determined to be closest to a pure resistance is identified as a preferred stimulation frequency. The stimulator **818** is then adjusted to provide a stimulation signal at a frequency, or frequency band, at or near the preferred stimulation frequency. The stimulation signal is then applied to the microelectrode array **815**.

Illustrated in FIG. **40** is an electronic circuit schematic diagram for an exemplary on board ASIC as shown in the embodiments above. Shown along the right hand portion of the schematic diagram are eight stimulation electrode elements **968***a* through **968***h* (generally **968**) which are generally spread between several cortical depth probes. Each one of these elements **968** is in electrical communication with a respective electronic device contact **974***a* through **974***d* and **974***m* through **974***p* (generally **974**). Also illustrated along the right hand portion of the schematic diagram are eight recording electrode elements **969***a* through **969***h* (generally **969**). Similarly, the recording contacts are spread between several cortical depth electrodes. Similarly, each of the recording electrode elements **970** is in electrical communication with a respective electronic device contact **974***e* through **974***h* and **974***j* through **974***l*. For illustrative purposes, the schematic diagram includes a representative electronic device **980**. For brevity, the schematic diagram includes only eight recording and eight stimulation contacts but a full schematic diagram for many more contacts is similar. Additionally, or alternatively, some embodiments will only include recording electrodes. Additionally, or alternatively, some embodiments will only include stimulation electrodes. The electronic device may include one or more of a switch or router, a preamplifier, a signal conditioner, a multiplexer, and a controller. The electronic device **980** is in electrical communication with all sixteen of the electronic device contact elements **974***a* through **974***p*.

The electronic device **980** is in further communication with wire lead contacts **976***a* through **976***d* (generally **976**) that are embedded in the exemplary ribbon cable tether. In the illustrative example, the first wire lead contact **976***a* is used for supplying electrical power to the microelectronic device and/or one or more of the stimulation electrode elements **968**. The second wire lead contact **976***b* is used to provide an electrical ground contact. This ground contact **976***b* may include earth ground, another electrical ground within the system, such as a chassis ground of a medical device connected to the electronic device **980**, or simply a signal return line. A third wire

lead contact **976***c* corresponds to a control signal that may be used to provide control inputs from an operator or other medical device, to control configuration and/or operation of the electronic device **980**. Alternatively or in addition, the control signal contact **976***c* may be used for control signals from the electronic device **980** to another medical device. A fourth wire lead contact **976***d* corresponds to a signal contact as may be used for directing electrical activity detected by one or more of the recording electrode elements **969** to a recording or display device. Alternatively or in addition, the signal contact **976***d* may be used for directing electrical stimulation signals from another medical device to one or more of the stimulation electrode elements **968**.

A top view of an exemplary embodiment of a microelectrode assembly **920** is illustrated in FIG. **41**A. The assembly **920** includes an array of microelectrodes **922** positioned along a distal end of an elongated probe substrate **924**. A first electronic assembly **928** is positioned at a proximal end of the elongated probe substrate **924**. The first electronic assembly **928** can include one or more integrated circuit elements **921**, such as a microprocessor, and one or more discrete electronic components **932**. The first electronic assembly **928** is interconnected to each of the microelectrodes **922** through a respective trace **926** running along the elongated probe substrate **924**. The electronic assembly **928** and can be configured to implement one or more functions of the implantable neurological stimulator described herein. In some embodiments, the elongated probe substrate also includes at least a portion of the electronic assembly **928**.

In some embodiments, the first electronic circuitry **928** is connected to an implanted pulse generator (not shown) through a cable **924**. In some embodiments, as shown, a second electronics assembly (or a portion of the first electronics assembly) includes telemetry circuitry **939**, such as a telemetry antenna. In the exemplary embodiment, at least a portion of electronic circuitry **928**, **938** is positioned adjacent to the microelectrodes **922**, for example being joined by the elongated probe substrate **924**.

The mechanical components and associated assembly processes serve to house the assembly **920** in a hermetic and biocompatible manner. They may also enable connection to an existing Implantable Pulse Generator or the extra-corporeal control unit. The extra-corporeal unit can provide power, programming ability, and retrieval of information. In some embodiments, the assembly **920** can be implanted much like currently available external cochlear stimulation systems. In an embodiment that includes an implantable pulse generator, it would serve to retrieve information and program the electrical unit to route the signals from the implantable pulse generator to the microelectrode array **922**.

The device provides highly localized and efficient stimulation by incorporating microfabricated components, electronic components and mechanical components. The microfabricated component consists of a microelectrode array. This array can be implemented in a polymeric material such as polyimide, polyurethane, parylene, or polysiloxane (silicone) and includes thin film or plated layers of a metal or metal oxide with high charge transfer capability such as platinum, platinum-iridium, iridium, iridium oxide or titanium. The polymeric and metallic layers can be deposited sequentially and formed using established principles of microfabrication such as spin coating, DC/RF sputtering, photolithography, plasma etching, and etching with a mask consisting of a secondary or sacrificial material such as silicon dioxide or photosensitive resist. The metallic layer can be formed to create the microelectrode arrays and traces which connect the array to the electronics and housing. The polymeric layers serve to isolate the traces from each other but also provide the structure of the implant's stimulating/recording tip. There are several fabrication methods which can be described to build such a microfabricated component.

The electronic or microelectronic components of the device enable: (i) the ability to identify the peak resistance frequency for each individual microelectrode site using electrical impedance spectroscopy; (ii) stimulate at the characteristic peak resistance frequency of each microelectrode (this guarantees minimized signal distortion and maximum charge transfer to the tissue); and (iii) stimulation and modulation of neuronal activity with the microelectrode array and the ability to select which microelectrode sites are stimulating.

The electronics can be implemented using discrete components, integrated circuit technology, digital signal processing (DSP), or a combination of all three. The electronics can be incorporated in one unit, or can be used in conjunction with an existing implantable pulse generator (IPG). The electronics may include a telemetric programming interface to properly condition or route the signal from the IPG to the microelectrode array.

Referring to FIG. **41**B, a side view of an exemplary alternative embodiment of a microelectrode structure is illustrated. In this embodiment, an electronics assembly **956** is positioned remote from the microelectrode array **952**. The microelectrode array **952** is joined to the electronics assembly **956** through an arrangement of interconnecting electrical leads **954**. The electronics assembly **956** can be configured to implement one or more functions of the implantable neurological stimulator described herein. As illustrated, the electronics assembly **956** can also be connected to an implanted pulse generator (not shown) through an interconnecting cable **960**. Alternatively or in addition, the electronics assembly **956** can include telemetry circuitry for communicating with an external telemetry device **962**.

The electronics assembly can include an electrical grounding lead for interconnection to an electrical ground potential **958**. In any of the embodiments described herein, impedance measurements and/or stimulation can be implemented between two or more microelectrodes (e.g., adjacent microelectrodes). Alternatively or in addition, impedance measurements and/or stimulation can be implemented between one or more microelectrodes and an electrical ground reference.

Note that a device can be assembled to not include electronics. This device would then transfer the signal from the Implantable Pulse Generator directly to the electrodes. A device with electronics would first "pre-filter" the signal before applying to the electronics. This "pre-filter" might take the form of signal filtering in order to achieve a certain signal spectrum, multiplexing and routing in order to direct signals from a pulse generator to a choice of microelectrode sites. The following figures demonstrate the different components and embodiments.

Cortical Depth Probe Embodiments

Various exemplary embodiments of microelectrode array element configurations including tetrode arrangements are illustrated in FIG. **42**A through FIG. **42**D. Referring to FIG. **42**A, a microelectrode array element **1000** includes a stimulation electrode **1002** and four recording electrodes **1004**. In the exemplary embodiment, the stimulation electrode **1002** is disc-shaped; however, other shapes are anticipated, such as polygons, ovals, and irregular shapes. In this embodiment, the recording electrodes **1004** are substantially smaller than the stimulation electrode **1002**, and positioned within the outer perimeter of the stimulation electrode **1002**. In order to accommodate this arrangement, the stimulation electrode includes a respective open area **1006**, one for each of the

recording electrodes. In the exemplary embodiment, the recording electrodes **1004** are uniformly spaced having about 90° angular separation between adjacent pairs.

In general, the open areas **1006** can have any shape, and the shape need not be the same as the shape of any recording electrode **1004** that may be positioned therein. In the exemplary embodiments, the open areas **1006** do have a similar shape, namely a circle, as the disc-shaped recording electrodes **1004**. The openings are dimensioned larger than the recording electrodes **1004**, such that the recording electrodes can be placed within the open areas **1006**, without touching the stimulation electrode **1002**. An annular region of separation exists between the two electrodes **1002**, **1004**. The recording electrodes **1004** may each be similarly shaped and/or similarly sized with respect to each other. They may have similar shape as the stimulation electrode **1002**, or have a different shape. In some embodiments, at least some of the recording electrodes **1004** have different shapes and/or different sizes with respect to each other.

In the exemplary embodiment, the four disc electrodes **1004** embedded within the larger, stimulation electrode **1002**. The recording electrodes **1004** each have a respective diameter of about 50 μm, and a relative separation to their nearest neighbors of about 150 μm. The stimulation electrode has a diameter of 300 μm. In some embodiments, the diameter of each recording electrode can range between about 2 μm or less, and about 300 μm or more. In some embodiments, the diameter of the stimulation electrode can range between about 5 μm or less, and about 1,000 μm or more.

Referring to FIG. **42**B, an alternative embodiment of a microelectrode array element **1010** shows a stimulation electrode **1012** as a non-closed disc. The outer perimeter of the stimulation electrode **1012** generally follows a circular arc, with indentations defining open areas **1016** extending in from the perimeter, towards the center of the electrode **1012**. In particular, four such open areas **1016**, or slots, each accommodate a respective recording electrode **1014**. The recording electrode **1014** is positioned toward an inner end of the open area **1016**, nearest the center of the stimulation electrode **1012**. In at least some embodiments, the recording electrode **1014** is spaced apart from a perimeter of the open area **1016**, such that the recording electrode **1014** does not touch the stimulation electrode **1012**. In some embodiments, the perimeter of the stimulation electrode **1012** are generally rounded, without sharp corners, in order to prevent highly localized fields. Although a four-recording electrode embodiment is shown, other embodiments are possible including one or more recording electrodes positioned within respective open areas **1016**. Although circular shapes are illustrated for each of the stimulation electrode and the recording electrode, different shapes can be used. The shapes can be regular, such as ellipses, polygons, and irregular shapes.

Referring to FIG. **42**C, illustrates a similar embodiment of a microelectrode array element **1020** to that described above, except that two tetrodes **1024***a*, and **1024***b* are embedded within the same stimulation electrode **1022**. The two tetrodes **1024***a*, **1024***b* can record neural activity from different tissue volumes sizes, with different sensitivities to neural activity. The "inner tetrode" **1024***b* can have the same, or different microelectrode diameters than the "outer tetrode" **1024***a*. The diagram shows an "inner tetrode" with 50 μm discs, and an "outer tetrode" with 60 μm discs. Other shapes, sizes, and numbers of tetrode elements are possible.

Referring to another microelectrode element embodiment **1030** illustrated in FIG. **42**D, a tetrode **1034** is only slightly embedded into the stimulation electrode **1032**. As shown, the innermost portion of the open area **1036** is spaced apart from an outer perimeter of the stimulation electrode **1032** by a distance less than a diameter of the recording element **1034**. Such a configuration would allow adjustment and optimization of the sensitivity and volume of tissue being recorded.

Various embodiments of neurological stimulation devices and techniques have been described herein. These embodiments are given by way of example and are not intended to limit the scope of the present disclosure. It should be appreciated, moreover, that the various features of the embodiments that have been described may be combined in various ways to produce numerous additional embodiments.

One or more of any of the microelectrode array elements **1000**, **1010**, **1020**, **1030** can be positioned on an elongated planar member, or a cortical depth probe, forming a microelectrode array film that is one component of a neurological surface probe. The neurological surface probes described above were composed of at least one cortical depth probe. In most embodiments the cortical depth probe protrudes from a planar surface of the neurological surface probe. It is understood that the following embodiments, i.e., FIG. **43**A through **43**J, of cortical depth probes, can each be used and implemented in the embodiments of neurological surface probes presented herein.

A series of exemplary cortical depth probes are illustrated in FIG. **43**A through FIG. **43**J. An exemplary cortical depth probe **1040** is illustrated in FIG. **43**A. The cortical depth probe **1040** includes four microelectrode elements **1045**. Each of the microelectrode elements **1045** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the present embodiment microelectrode elements **1045** are implemented with a diameter of 300 um and are spaced by 1 mm. In the illustrative embodiment, the microelectrode elements **1045** are discoid and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

A series of exemplary cortical depth probes are illustrated in FIG. **43**A through FIG. **43**J. An exemplary cortical depth probe **1040** is illustrated in FIG. **43**A. The cortical depth probe **1040** includes four microelectrode elements **1045**. Each of the microelectrode elements **1045** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the present embodiment microelectrode elements **1045** are implemented with a diameter of 300 μm and are spaced by 1 mm. In the illustrative embodiment, the microelectrode elements **1045** are discoid and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

An additional cortical depth probe **1050** is illustrated in FIG. **43**B. The cortical depth probe **1050** includes three microelectrode elements **1055**. Each of the microelectrode elements **1055** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the present embodiment microelectrode elements **1055** are implemented with a diameter of 400 μm and are spaced by 1.5 mm. In the illustrative embodiment, the microelectrode elements **1055** are discoid and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

An additional cortical depth probe **1060** is illustrated in FIG. **43**C. The cortical depth probe **1060** includes two small diameter microelectrode elements **1065** and two large diameter microelectrode elements **1066**. Each of the microelectrode elements **1065** and **1066** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. However, in the present embodiment it may be preferable to use the small diameter microelectrode elements **1065** as recording electrodes because they are smaller in diameter and may capture more single-unit cellular activity.

Additionally, it may be preferable to use the large diameter microelectrode elements **1066** as stimulation electrodes because they are larger in diameter and can transfer more charge to the neural tissue increasing the efficacy of stimulation. In the present embodiment, small diameter microelectrode elements **1065** are implemented with a diameter of 300 μm, and large diameter microelectrode elements **1066** are implemented with a diameter of 700 μm. The microelectrode elements **1065** and **1066** are spaced by 1.2 mm. In the illustrative embodiment, the microelectrode elements **1065** and **1066** are discoid and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

Another alternative embodiment of a cortical depth probe **1070** is illustrated in FIG. **43**D. In this embodiment, each of the cortical depth probes **1070** include at least one elongated microelectrode elements **1075**. Each of the elongated microelectrode elements **1075** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the illustrative embodiment, the elongated microelectrode elements **1075** are rounded-corner rectangular and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

Another alternative embodiment of a cortical depth probe **1080** is illustrated in FIG. **43**E. In this embodiment, each of the cortical depth probes **1080** include at least one elongated microelectrode elements **1085** and one discoid microelement **1086**. Each of the microelectrode elements **1085** and **1086** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. However, in the present embodiment it may be preferable to use the discoid microelectrode elements **1085** as recording electrodes because they are smaller in diameter and may capture more single-unit cellular activity. Additionally, it may be preferable to use the elongated microelectrode elements **1086** as stimulation electrodes because they are larger in diameter and can transfer more charge to the neural tissue increasing the efficacy of stimulation. In the illustrative embodiment, the microelectrode elements **1085** and **1086** spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

An exemplary cortical depth probe **1090** is illustrated in FIG. **43**F. The cortical depth probe **1090** includes four microelectrode elements **1095**. Each of the microelectrode elements **1095** includes a respective stimulation electrode **1092** and tetrode arrangement of recording electrodes **1094**. In the illustrative embodiment, discoid tetrode elements **1094** are disposed along an external perimeter of a discoid stimulation electrode **1092**, such that the tetrode elements **1094** are spaced apart from the outer perimeter of the stimulation electrode **1092**.

Another alternative embodiment of a cortical depth probe **1100** is illustrated in FIG. **43**G. In this embodiment, each of the cortical depth probes **1100** include four microelectrode elements **1105**. Each of the microelectrode elements **1105** includes a respective stimulation electrode **1102** and tetrode arrangement of recording electrodes **1104**. In the illustrative embodiment, discoid tetrode elements **1104** are disposed within an open interior region of an annular stimulation electrode **1102**, such that the tetrode elements **1104** are spaced apart from the inner annular perimeter of the stimulation electrode **1102**.

Another alternative embodiment of a cortical depth probe **1110** is illustrated in FIG. **43**H. In this embodiment, each of the cortical depth probes **1110** include four microelectrode elements **1115**. Each of the microelectrode elements **1115** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the illustrative embodiment, the microelectrode elements **1115** are rectangular and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

Another alternative embodiment of a cortical depth probe **1120** is illustrated in FIG. **43**I. In this embodiment, each of the cortical depth probes **1120** include at least one microelectrode element group **1125**. In the present embodiment there are four microelectrode element group **1125**. Each of the microelectrode element groups **1125** is composed of at least one rectangular microelectrode sub-element **1122**. In this present embodiment there are four rectangular microelectrode sub-elements **1122** in each of the microelectrode element groups **1125**. In some embodiments the four rectangular microelectrode sub-elements **1122** are all connected electrically, taking advantage of the edge effects to perform more efficient neurostimulation. In some embodiments the four rectangular microelectrode sub-elements **1122** are not connected electrically, and are independently stimulated. Microelectrode element groups **1125** in addition to collective, or individual, microelectrode sub-elements **1122** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the illustrative embodiment, the microelectrode element groups **1125** are rectangular groups of microelectrode sub-elements **1122** and are spaced apart from each other in a manner to cover a wide linear depth in the cortical region.

Another alternative embodiment of a cortical depth probe **1130** is illustrated in FIG. **43**J. In this embodiment, each of the cortical depth probes **1130** includes at least one graded microelectrode element group **1135**. Each of the graded microelectrode element groups **1135** is composed of at least one rectangular microelectrode sub-element, collectively **1132**. In this present embodiment there are five rectangular microelectrode sub-elements **1132** in each of the graded microelectrode element groups **1135**. The rectangular microelectrode sub-elements **1132** decrease in width and spacing towards the center of a graded microelectrode element group **1135**. For example, in this manner, electrical stimulation performed can focus current to the center of such a group, while maintaining advantageous and safe electrochemical limits. For example, microelectrode sub-element **1132***a* is 300 μm wide, microelectrode sub-element **1132***b* is 100 μm wide, and microelectrode sub-element **1132***c* is 50 μm wide. In some embodiments the rectangular microelectrode sub-elements **1132** are all connected electrically, taking advantage of the edge effects to perform more efficient neurostimulation. In some embodiments the rectangular microelectrode sub-elements **1132** are not connected electrically, and are independently stimulated. Graded microelectrode element groups **1135** in addition to collective, or individual, microelectrode sub-elements **1132** can be used as stimulation or recording electrodes, or combined stimulation-recording electrodes. In the illustrative embodiment, there are two graded microelectrode element groups **1135** of microelectrode sub-elements **1132** but it is understood that more can be implemented.

In practice the operator can connect the neurological surface probe **101** to a recorder unit configured to identify certain regions of the neurological target (e.g., the brain) according to the electrical activity detected by the microelectrode elements shown in FIG. **43**A through FIG. **43**J. In some embodiments, the microelectrode elements used to record from the neurological target can be the same microelectrodes as those used to stimulate the target in applications in which both recording and stimulation are accomplished. Alternatively or in addition, the microelectrode elements used to record from the neurological target can be separate microelectrode elements from those used to stimulate the target. This is demon-

strated in embodiments, where each cortical depth probe includes one or more recording electrodes and one or more stimulating electrodes. As shown, the dedicated recording electrodes are smaller than dedicated stimulation electrodes. In some embodiments, microelectrodes destined for recording may differ in one or more of size, shape, number, and arrangement from those microelectrodes destined for stimulation, e.g., using different microelectrodes.

CONCLUSION

Various embodiments of micro-fabricated cortical neuromodulation devices have been described herein. These embodiments are giving by way of example and are not intended to limit the scope of the present disclosure. It should be appreciated, moreover, that the various features of the embodiments that have been described may be combined in various ways to produce numerous additional embodiments. Moreover, while various materials, dimensions, shapes, implantation locations, etc. have been described for use with disclosed embodiments, others besides those disclosed may be utilized without exceeding the scope of the disclosure.

Although some devices described herein are identified as either cutaneous or chronic, it is understood that such cutaneous devices may be used in chronically, being implanted for extended periods, or even indefinitely. Similarly, any devices described herein as being chronic, it is understood that such devices may also be used cutaneously.

All definitions, as defined and used herein, should be understood to control over dictionary definitions, definitions in documents incorporated by reference, and/or ordinary meanings of the defined terms.

The indefinite articles "a" and "an," as used herein in the specification and in the claims, unless clearly indicated to the contrary, should be understood to mean "at least one."

The phrase "and/or," as used herein in the specification and in the claims, should be understood to mean "either or both" of the elements so conjoined, i.e., elements that are conjunctively present in some cases and disjunctively present in other cases. Multiple elements listed with "and/or" should be construed in the same fashion, i.e., "one or more" of the elements so conjoined. Other elements may optionally be present other than the elements specifically identified by the "and/or" clause, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, a reference to "A and/or B", when used in conjunction with open-ended language such as "comprising" can refer, in one embodiment, to A only (optionally including elements other than B); in another embodiment, to B only (optionally including elements other than A); in yet another embodiment, to both A and B (optionally including other elements); etc.

As used herein in the specification and in the claims, "or" should be understood to have the same meaning as "and/or" as defined above. For example, when separating items in a list, "or" or "and/or" shall be interpreted as being inclusive, i.e., the inclusion of at least one, but also including more than one, of a number or list of elements, and, optionally, additional unlisted items. Only terms clearly indicated to the contrary, such as "only one of" or "exactly one of," or, when used in the claims, "consisting of," will refer to the inclusion of exactly one element of a number or list of elements. In general, the term "or" as used herein shall only be interpreted as indicating exclusive alternatives (i.e., "one or the other but not both") when preceded by terms of exclusivity, such as "either," "one of," "only one of," or "exactly one of." "Consisting essentially of," when used in the claims, shall have its ordinary meaning as used in the field of patent law.

As used herein in the specification and in the claims, the phrase "at least one," in reference to a list of one or more elements, should be understood to mean at least one element selected from any one or more of the elements in the list of elements, but not necessarily including at least one of each and every element specifically listed within the list of elements and not excluding any combinations of elements in the list of elements. This definition also allows that elements may optionally be present other than the elements specifically identified within the list of elements to which the phrase "at least one" refers, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, "at least one of A and B" (or, equivalently, "at least one of A or B," or, equivalently "at least one of A and/or B") can refer, in one embodiment, to at least one, optionally including more than one, A, with no B present (and optionally including elements other than B); in another embodiment, to at least one, optionally including more than one, B, with no A present (and optionally including elements other than A); in yet another embodiment, to at least one, optionally including more than one, A, and at least one, optionally including more than one, B (and optionally including other elements); etc.

In the claims, as well as in the specification above, all transitional phrases such as "comprising," "including," "carrying," "having," "containing," "involving," "holding," "composed of," and the like are to be understood to be open-ended, i.e., to mean including but not limited to. Only the transitional phrases "consisting of" and "consisting essentially of" shall be closed or semi-closed transitional phrases, respectively, as set forth in the United States Patent Office Manual of Patent Examining Procedures, Section 2111.03

While this disclosure has been particularly shown and described with references to various embodiments, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the scope of the encompassed by the appended claims.

What is claimed is:

1. An implantable neurological probe comprising:

a supportive backing layer; and

a flexible substrate disposed on the supportive backing layer and comprising an insulative layer, a conductive layer comprising one or more conductive traces disposed on the insulative layer, at least one microelectrode element disposed on the insulative layer and coupled to the one or more conductive traces, and a second insulative layer disposed on the conductive layer.

2. The implantable neurological probe of claim **1**, further comprising at least one protrusion, the at least one microelectrode element disposed thereon.

3. The implantable neurological probe of claim **2**, wherein a length of the at least one protrusion is not more than about 4 mm.

4. The implantable neurological probe of claim **1**, comprising at least one feature to promote flexibility of the supportive backing layer.

5. The implantable neurological probe of claim **3**, wherein the at least one feature includes an aperture promoting flexibility in a preferred direction.

6. The implantable neurological probe of claim **1**, comprising a plurality of microelectrode elements, wherein at least one of the plurality of microelectrode elements is shaped substantially different from another microelectrode element of the plurality of microelectrode elements.

7. The implantable neurological probe of claim **1**, comprising a plurality of microelectrode elements, wherein the plurality of microelectrode elements comprise at least one stimulating electrode and at least one detecting electrode.

8. The implantable neurological probe of claim 7, wherein the at least one stimulating electrode is shaped substantially different from the at least one detecting electrode.

9. The implantable neurological probe of claim 8, wherein the at least one of the stimulating electrode and the at least one detecting electrode comprises a plurality of electrically conducting sub-elements.

10. The implantable neurological probe of claim 9, wherein the at least one of the stimulating electrode and the at least one detecting electrode comprises a tetrode arrangement of electrically conducting sub-elements.

11. The implantable neurological probe of claim 1, wherein the at least one microelectrode element is configured as a micro-electromechanical system (MEMS).

12. The implantable neurological probe of claim 1, further comprising at least one electronic circuit element in electrical communication with the at least one microelectrode element.

13. The implantable neurological probe of claim 1, wherein the at least one electronic circuit element comprises at least one of a switch; a router; an amplifier; a controller; a microprocessor; memory; a multiplexer; a filter; an attenuator; a resistor; a capacitor; an inductor; a diode; a transistor; and combinations thereof.

14. The implantable neurological probe of claim 1 wherein the supportive backing layer is semi-rigid.

15. The implantable neurological probe of claim 1, wherein the supportive backing layer includes medical grade stainless steel.

16. A method for stimulating a neurological target comprising:

implanting a neurological probe within a vicinity of a neurological target site, the neurological probe comprising a supportive backing layer and a flexible substrate disposed on the supportive backing layer, the flexible substrate comprising an insulative layer, a conductive layer comprising one or more conductive traces disposed on the insulative layer, at least one microelectrode element disposed on the insulative layer and coupled to the one or more conductive traces, and a second insulative layer disposed on the conductive layer; and

energizing by a supplied electrical signal, the at least one microelectrode element, wherein the at least one microelectrode element produces an electric field adapted to stimulate the neurological target site.

17. The method of claim 16, wherein the act of implanting comprising:

positioning a surface of the supportive backing layer along a surface of a brain.

18. The method of claim 16, further comprising:

recording neurological activity detected by the at least one microelectrode element; and

repositioning the neurological probe as required, until the recorded activity is indicative of the neurological probe being located sufficiently at the neurological target site.

19. The method of claim 16, wherein the supplied electrical signal is obtained from an implanted pulse generator.

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